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THE PRINCIPLES AND TECHNIQUE OF RESECTION OF SOFT PARTS FOR SARCOMA

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NO TYPE of neoplasm is more indifferently treated in contemporary surgical practice than is the sarcoma of soft tissue origin. This is explained in part by the fact that these tumors are relatively uncommon and are infrequently encountered by the individual surgeon. It is explained in part by the unfamiliarity of many surgeons with the usual characteristics and behavior of these neoplasms. Knowledge of these factors convincingly demonstrates the need for aggressive and adequate treatment which, when carried out, is followed by sufficiently good results in a significant number of cases to make the endeavor well worth while. This fact has led some surgeons in recent years to employ primary amputation as the treatment of choice for sarcomas of the extremities.

While in no sense intending to deprecate amputation as a means of treatment in certain situations, we herewith submit a method of surgical treatment which is consistent with the natural behavior of these tumors, which satisfies the tenets of good cancer surgery, and which obviates in selected instances the loss of an extremity. This approach to the surgical treatment of sarcomas of the soft tissues is based upon our experience in the management of 36 such tumors, either directly in our own practices or indirectly in the wards and clinic of the Mixed Tumor Service of the Memorial Hospital. The principles and technique herein described are not original but are derived from the precepts of Dr. George T. Pack, Chief of the Mixed Tumor Service at Memorial Hospital, and from the many contributions of Dr. Arthur Purdy Stout to the understanding of the pathology and clinical behavior of these tumors.

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PRINCIPLES

Sarcomas of the soft parts are believed, in most instances, to start *de novo* in muscle, fascia, nerve sheath, fat, and so forth as a nidus of actively proliferating cells resembling in varying degree the parent tissue from which they arise.* No capsule surrounds these cells. They are in direct contact with surrounding normal tissue and, like other malignant cells, directly invade these surrounding tissues. In certain rapidly growing tumors the peripherally situated neoplastic cells may be so flattened as to form a "pseudocapsule." When , because of this pseudocapsule, sarcomas are simply enucleated, scattered foci of residual tumor are inevitably left behind in the tumor bed and local recurrence is a certainty! Ivins and associates[5] noted one or more local recurrences of fibrosarcoma after simple local excision in 63 per cent of their patients who were subsequently cured and in 94 per cent of their patients who died. Stout[9] reported a 60 per cent local recurrence rate in his series of patients with fibrosarcoma. Clark and associates[3] showed that, of 85 patients who had local excisions for sarcomas of the soft parts, 31 patients had one recurrence and 21 had multiple recurrences, whereas only 2 of 21 patients treated primarily by radical resection of soft tissue had local recurrences. Lieberman and Ackerman[6] describe 15 patients with recurrence following simple excision in a group of 27 patients with fibrosarcoma and 15 similar local recurrences in 31 patients with liposarcoma. Pack and Pierson[8] in their series of 105 patients with liposarcoma report a 33 per cent incidence of recurrent operable liposarcoma at the time of first examination of these patients.

The ineffective initial operative results for rhabdomyosarcoma are shown by the finding that almost half of these tumors treated at Memorial Hospital[7] had locally recurrent lesions when first seen. Stout[12] reported that 66 of 108 patients with rhabdomyosarcoma had local recurrence following an initial attempt at curative treatment.

Common surgical practice, however, still condones simple local excision, frequently supplemented by roentgen therapy employed in the hope of destroying any residual neoplastic tissue that may remain. Even if the tumor bed could be completely cleared of neoplastic cells by such illogical treatment, a second characteristic of sarcoma of the soft parts is thus overlooked: These tumors are apt to extend directly within muscle bundles, along nerve sheaths,[1] or along contiguous fascial planes well beyond the confines of visible and palpable tumor. There is, furthermore, evidence that certain of these tumors may arise in multicentric foci within a muscle belly. Stout[10] reported 6 of 31 patients with multicentric foci of liposarcoma and emphasized that multiple foci of sarcoma frequently accounted for local recurrence. The operative procedure must include wide ablation of surrounding grossly normal tissue so that no actual tumor is exposed during its removal. Entire muscle bundles surrounding the sarcoma must be removed at points of origin and insertion. The procedure

*The possibility of "malignant degeneration" in a previously existing benign lesion is not necessarily rejected, but a discussion of this thesis is not pertinent to the exposition of the present subject matter.

must be carried out by sharp dissection with handling and massage of the tumor reduced to an absolute minimum and with proximal ligation of the major venous tributaries carried out early in the procedure. It possibly should include, in certain instances, removal of the regional lymph nodes when it is feasible anatomically and should always include regional lymph-node dissection if the presence of node metastasis is strongly suspected or seriously anticipated.

Depending, therefore, upon the anatomic location of the sarcoma, adequate surgical treatment may require amputation in certain instances or may be accomplished by extensive resection of the soft parts in other instances. There is a natural tendency to perform small operations for relatively low-grade tumors and extensive operations for the highly aggressive ones. A local procedure will often be advised for a fascial fibrosarcoma while a radical exarticulation will more likely be advised for the highly malignant synovial sarcoma. Such *histologic* criterion for the choice of surgical procedure is at present unchallenged but is at present unfounded on the basis of known results, although Ghormley's[4] opinion is to the contrary.

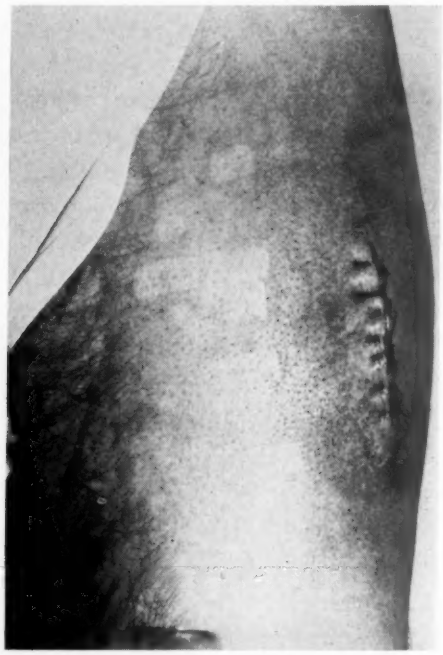
In our opinion, the criterion for the choice of surgical procedure should be the *gross anatomic setting* of the tumor. An extensive resection of soft tissue should be carried out for a sarcoma, regardless of histogenesis, when complete removal of the tumor and its surrounding muscles, fat fascia, and skin can be readily accomplished. Amputation should be performed for a sarcoma, regardless of histogenesis, when, because of proximity to bone, joint, or principal vessels, the tumor cannot otherwise be adequately removed. Thus, even a small sarcoma arising around the wrist will probably require amputation while a much larger sarcoma arising in the muscles of the mid-thigh may be adequately resected with preservation of the leg.

TECHNIQUE

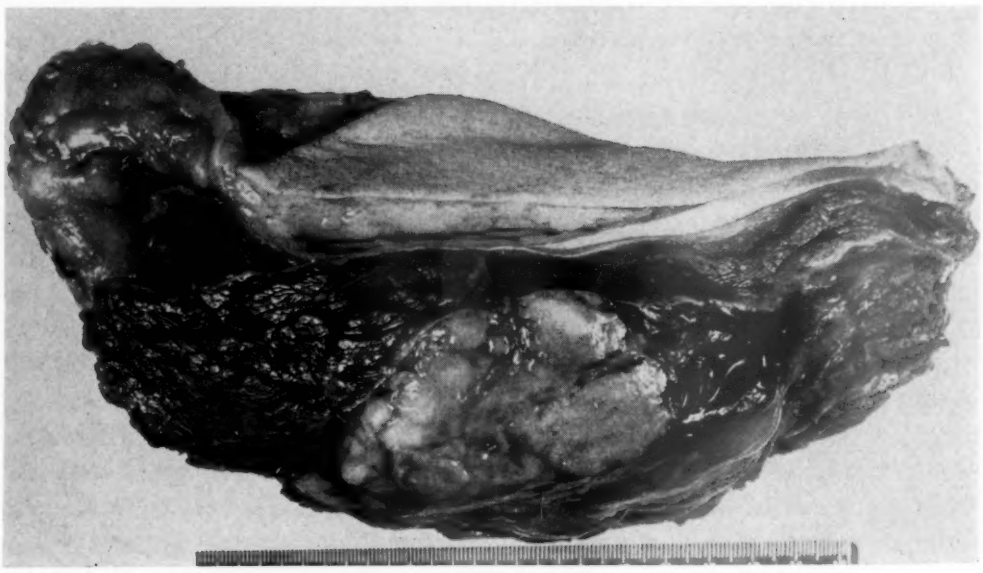
Obviously no single technique for conservative resection of sarcomas of soft tissue is feasible because of the wide variation in site of origin of these lesions. For the purpose of description, however, the technique actually employed in two of our cases, one a rhabdomyosarcoma of the thigh and the other a fibrosarcoma of the arm, is herewith presented in detail. It should be realized that the exact location and extent of a sarcoma cannot be determined by preoperative findings but is positively determined only by anatomic dissection of the surgical specimen after removal. Thus, in both of the following descriptions it may be suggested that incisions were overly generous and that certain structures were unnecessarily sacrificed. Both procedures exemplify the practice of block excision of muscle bundles at points of origin and insertion, the practice of sharp dissection through grossly normal tissue at all points of the procedure, and the practice of proximal incision and prompt ligation of venous tributaries early in the procedure. The first case also exemplifies the practice of regional node dissection-in-continuity which was employed here because of anatomic feasibility.

CASE REPORTS

CASE 1.—S. S., a 55-year-old man, had rhabdomyosarcoma of the left lateral thigh measuring 10 by 9 by 5 cm. Diagnosis had been elsewhere established by incisional biopsy through a 7.5 cm. incision overlying the tumefaction (Fig. 1, *A*).



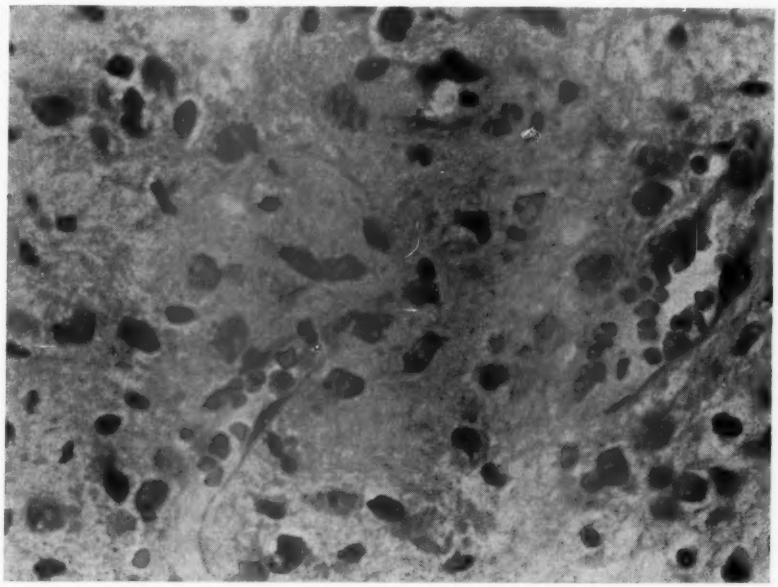
A.



B.

Fig. 1.—S. S., a 55-year-old man with rhabdomyosarcoma. *A*, Biopsy incision overlying tumefaction of left thigh. *B*, Gross surgical specimen following radical soft-tissue resection. *C*, Photomicrograph (×320) showing histologic structure of tumor. *D*, Postoperative appearance of wound, showing healed pinch grafts and loss of soft tissue substance.

Curvilinear incision was made from the left costal arch vertically downward across the inguinal ligament onto the anterior thigh and downward to the lateral aspect of the knee. A counter-incision was made from the abdominal portion of the first incision, extended laterally in curving fashion over the hip well onto the posterolateral aspect of



C.

D.

Fig. 1 Cont'd.—*For legend see opposite page.*

the thigh, and then directed anteriorly again to join with the first incision over the lateral aspect of the knee. The generous skin ellipse thus outlined passed on either side of the palpable tumor and contained in its center the sutured biopsy incision (Fig. 2).

Superficial inguinal node dissection was carried out, dissecting lateral and medial abdominal skin flaps, mobilizing subcutaneous tissue overlying the inguinal canal, and reflecting this tissue downward over Poupart's ligament. Incision was then made through the full thickness of the abdominal musculature from the costal arch to the anterior superior iliac spine where Poupart's ligament was detached and the anterior abdominal wall retracted medially and superiorly. The underlying peritoneum could then be retracted medially to expose the retroperitoneal space and to permit deep iliac, hypogastric, and obturator node dissection. The node-bearing tissue from the retroperitoneum was thus dissected caudad to join with that previously mobilized from the superficial inguinal area at the point of emergence of the femoral vessels under Poupart's ligament. In the course of this dissection, the hypogastric vein was ligated in continuity at its junction with the external iliac vein, and the other tributaries, both arterial and venous, of the iliac vessels including the inferior epigastric, circumflex iliac, and circumflex femoral vessels were ligated and divided. The abdominal wall was reconstituted then with a double layer of interrupted sutures and Poupart's ligament was resutured to the anterior superior iliac spine.

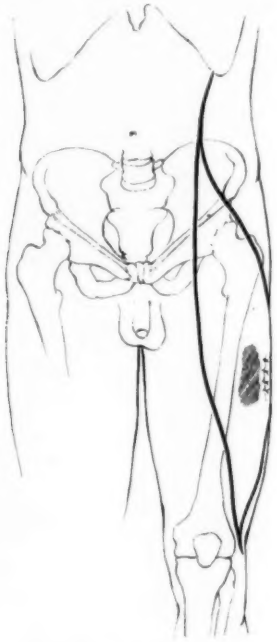


Fig. 2.

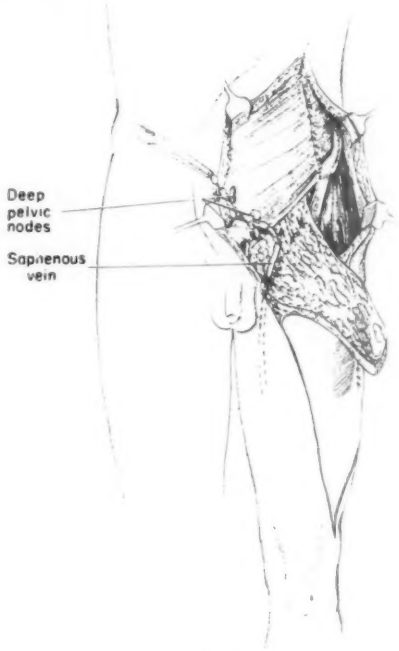


Fig. 3.

Fig. 2.—Diagram indicating location of tumor and lines of incision in Patient S. S. (Fig. 1).

Fig. 3.—Retroperitoneal node dissection has been completed with the chain of deep pelvic nodes mobilized and lifted up for demonstration. The abdominal wall musculature has been reconstituted and the divided inguinal ligament sutured back to the iliac spine.

The lateral skin flap, already dissected back over the abdomen, was further dissected laterally throughout its full extent to expose the anterior half of the iliac crest and the lateral musculature of the thigh. The medial skin flap was further reflected to expose the fatty node-bearing tissue over the femoral triangle (Fig. 3).

Note that up to this point the sarcoma itself had not been palpated, massaged, or even closely approached but the proximal venous tributaries had been secured with the exception of the common femoral vein.

Incision was made with the scalpel along the exposed iliac crest to divide the tensor fasciae latae and the gluteus medius muscles at their point of origin. The anterior border of the gluteus maximus was separated by sharp dissection from the gluteus medius and retracted posteriorly. As the tensor fasciae latae and gluteus medius muscles were retracted downward, the superior gluteal vessels, emerging above the pyriformis tendon, could

be secured and divided. The fascia lata was incised along its posterior edge dividing that portion of the tendon of the gluteus maximus which inserts here, and the gluteus medius was again divided at its point of insertion on the greater trochanter of the femur. As the gluteus medius and tensor fasciae latae muscles were mobilized from the hip, it became apparent that the tumor lay still more deeply in the substance of the vastus lateralis muscle. The biceps femoris muscle therefore was retracted posteriorly and the extensive origin of the vastus lateralis muscle on the lateral surface of the femur was divided after incising the lateral septal fascia at its attachment on the linea aspera of the femur. The lateral and posterior planes of resection were thus accomplished (Fig. 4).

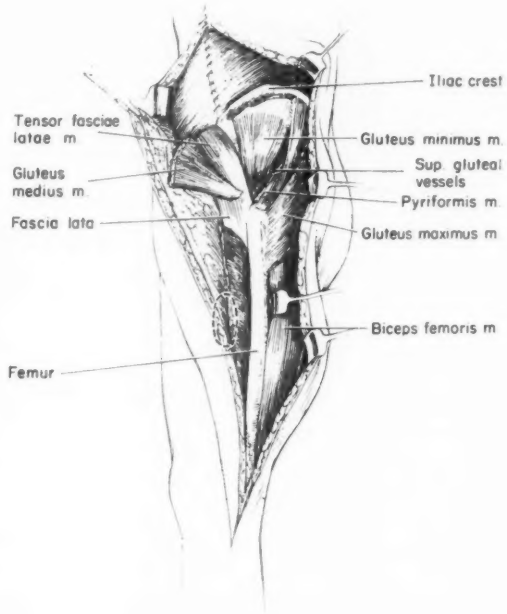


Fig. 4.—Lateral aspect of the operative field after division of the gluteus medius, tensor fasciae latae, and the vastus lateralis muscles at their points of origin. The superior, lateral, and posterior planes of dissection have been completed.

The node-bearing tissue of the femoral area was meticulously dissected from the femoral vessels and nerve and, along with the superficial and deep inguinal contents, was reflected laterally toward the tumor lying deep within the lateral musculature of the thigh. The quadriceps femoris and sartorius muscles underlying were exposed throughout their full length. The surgeon's hand could be passed under the already mobilized vastus lateralis muscle, and with gentle traction outward its insertion into the patellar tendon was divided and the muscle as a whole split from the rest of the quadriceps group by sharp dissection (Fig. 5). The specimen was freed thus from the thigh and removed. The space beneath the inguinal ligament was closed with interrupted sutures as in a standard femoral hernia repair and, after drains were placed, the sizeable operative defect (Fig. 6) was covered readily with minimal tension by suturing the skin flaps together.

Comment: In retrospect, it is obvious that the gluteus muscle could have been spared but this could not be determined by the operator at the start of the dissection. Furthermore, the absence of node metastasis in the groin contents, as proved by pathologic study, implies that the groin dissection may have been an unnecessary extension of the operative procedure. However, the fact that the patient is living and well and economically rehabilitated 6½ years following the surgery implies that the procedure as carried out was therapeutically effective.

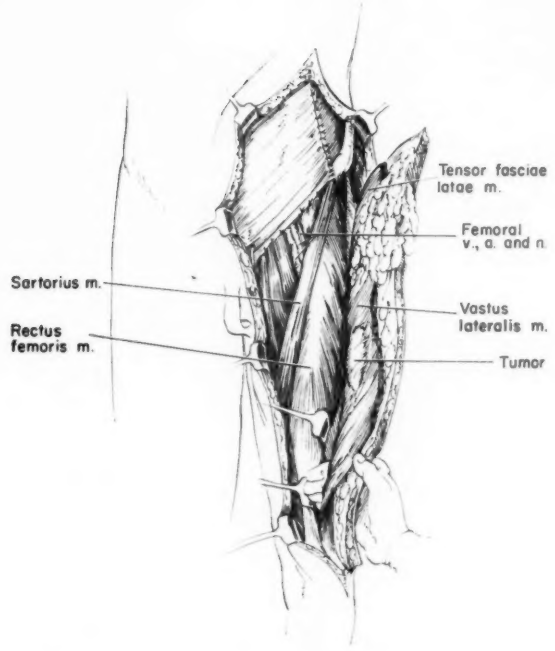


Fig. 5.—Anterior aspect of the operative field showing a completed groin dissection with inguinal and femoral nodes attached to the specimen and displaced laterally and showing mobilization of the vastus lateralis just prior to its division at its point of insertion into the patellar tendon.

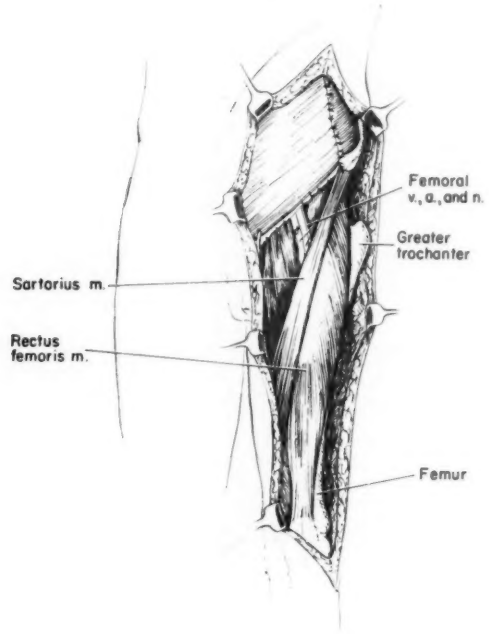


Fig. 6.—Extensive operative defect resulting from the radical soft-tissue resection of a rhabdomyosarcoma of the vastus lateralis already described.

CASE 2.—D. C., a 17-year-old man, had fascial fibrosarcoma of the left arm measuring 8.5 by 6.5 cm. Diagnosis of sarcoma was established preoperatively by needle biopsy (Fig. 7, *A*).

A generous elliptical incision was made around the palpable tumor in the lateral aspect of the left arm beginning over the acromion and extending down to the lateral epicondyle of the humerus (Fig. 8). The anterior skin flap was developed to expose the deltopectoral groove and the anterior surface of the biceps muscle. A posterior skin flap was developed to expose the outer half of the trapezius muscle, the posterior border of the deltoid muscle, and the long head of the triceps muscle. The extensive origin of the deltoid muscle was incised and the deltoid was removed from the clavicle, acromion, and spine of the scapula. The deltopectoral groove was entered and the deltoid muscle separated by sharp dissection from the pectoralis major tendon. Incision was continued downward in this plane and a portion of the biceps muscle in close approximation to the palpable tumor was sharply incised throughout the length of the muscle and divided through its tendinous insertion from the main muscle bundle. Incision was similarly made over the posterior edge of the deltoid muscle, mobilizing it and exposing the underlying supraspinatus, infraspinatus, and teres minor tendons. The deeper-lying long head of the triceps muscle could be retracted medially and posteriorly but the lateral head of the triceps was divided at its origin on the shaft of the humerus. The radial nerve, lying in the spiral groove of the humerus just below the origin of the lateral head of the triceps was exposed, indentified, and preserved carefully. At this point the humeral circumflex vessels were transected and ligated and the anterior branch of the axillary nerve was cut. By traction laterally and forward on the lateral head of the triceps, this muscle belly was divided from the rest of the triceps by splitting the common tendon of insertion and transecting its outer third (Fig. 9).

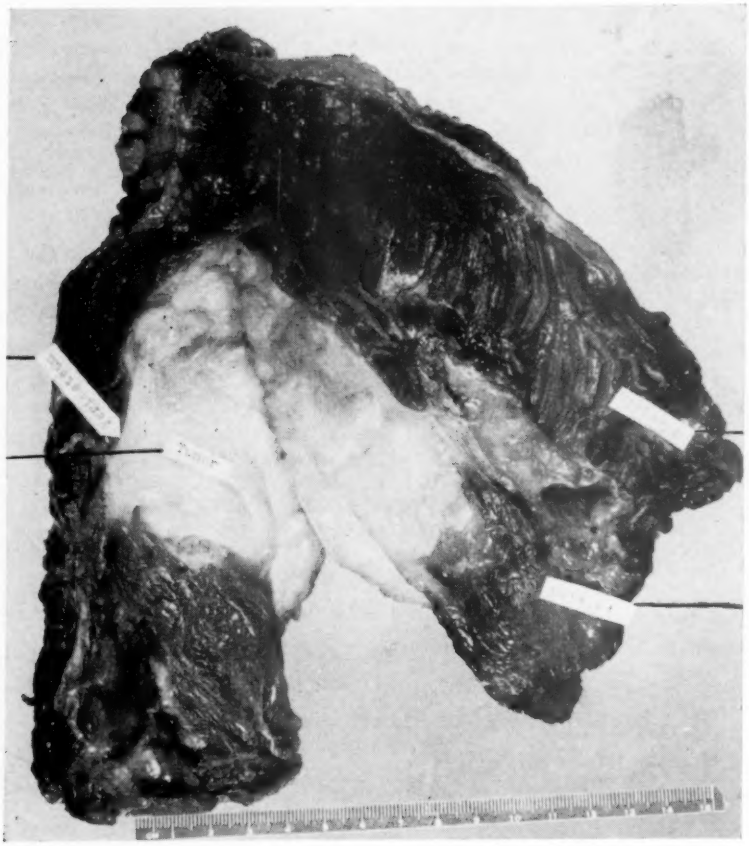
The specimen to be removed was mobilized except for the insertion of the deltoid immediately deep to the palpable tumor. Because of proximity of the tumor at this point, the otherwise mobilized deltoid muscle was retracted outward, the periosteum of the outer surface of the humerus was incised just above the deltoid tuberosity, and, with mallet and osteotome, a segment of periosteum and bone, including the deltoid tuberosity, was shaved from the cortex of the humerus. The specimen removed, containing the tumor in its midst, consisted of an ellipse of skin and subcutaneous tissue, the entire deltoid muscle, a longitudinal strip of biceps muscle, the lateral head of the triceps muscle, and a small plaque of cortical bone. The operative defect (Fig. 10) was closed by plicating the long head of the triceps muscle over the musculospiral groove to cover the radial nerve, and, after drains were placed, the skin flaps were approximated and a bulky pressure dressing was applied.

Comment: The length of the incision, in retrospect, was probably greater than necessary but afforded excellent exposure for precise resection of muscle bundles. This patient is living and well with minimal disability 36 months following his operation.

DISCUSSION

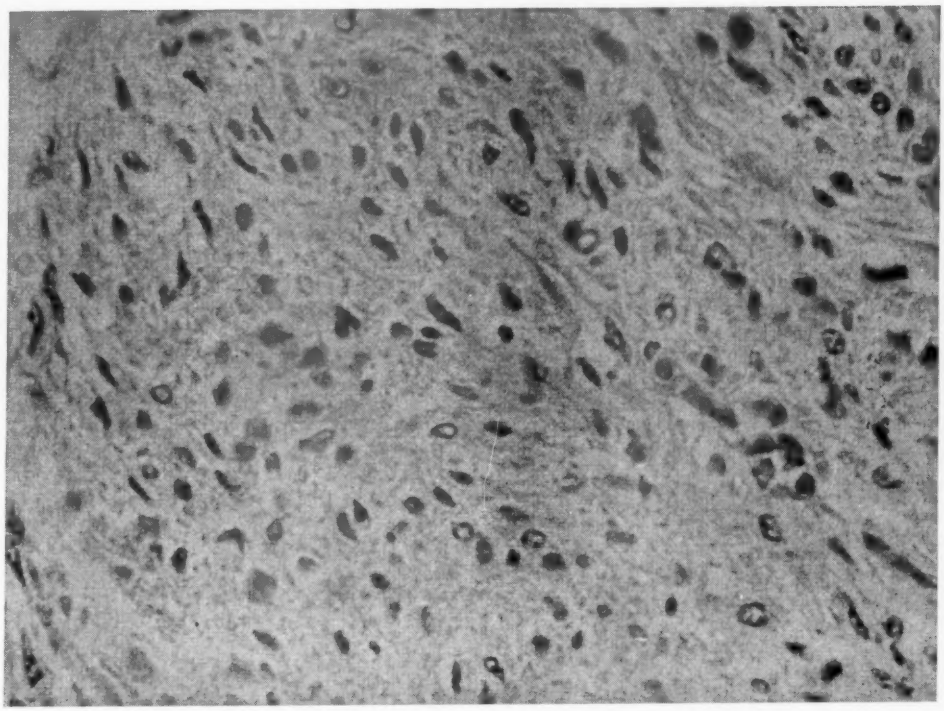
It should be emphasized again that extensive resection of soft parts is not applicable to all sarcomas of soft parts. For example, the recent study of Barber and associates[1] indicating that 11 of 98 extremities amputated for sarcomas of soft parts showed that invasion of adjacent peripheral nerves is sound argument against this conservative operation in management of those tumors located close to major nerve trunks. However, when a sarcoma is so situated anatomically that wide removal of the tumor can be carried out as described, amputation of the involved extremity may not be necessary. The validity of this proposition should rest on one criterion, namely, the presence or absence of subsequent local recurrence. The subsequent development of pulmonary or other distant metastases when the primary site remains free of cancer cannot

A.



B.

Fig. 7.—*For legend see opposite page.*



C.

D.

Fig. 7 Cont'd.—D. C., a 17-year-old youth with fibrosarcoma. *A*, The tumefaction of the left upper extremity is here shown. *B*, Gross surgical specimen following radical soft-tissue resection. *C*, Photomicrograph (×160) showing histologic structure of tumor. *D*, Postoperative appearance of wound showing extent of incision and loss of soft tissue substance.

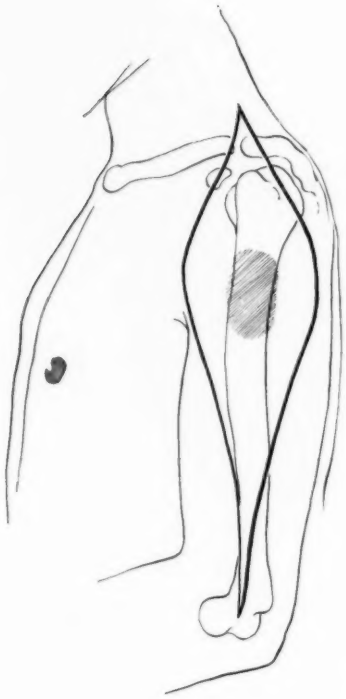


Fig. 8.

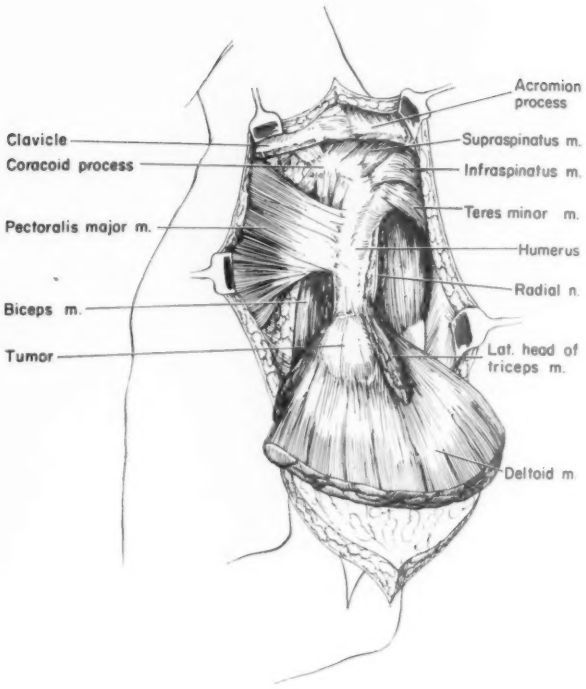


Fig. 9.

Fig. 8.—Diagram indicating location of tumor and lines of incision in Patient D. C. (Fig. 7).

Fig. 9.—Operative field after mobilization of deltoid muscle containing the tumor, showing proximity of tumor to the point of insertion of the deltoid into the humerus.

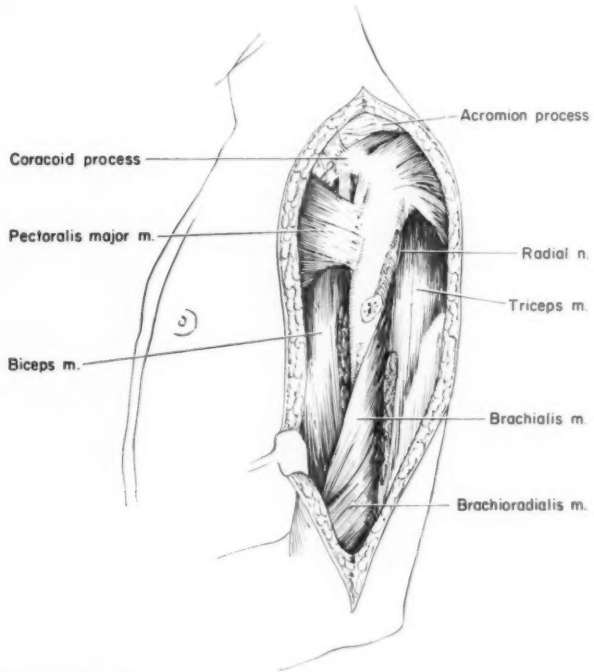


Fig. 10.—Extensive operative defect resulting from the radical soft-tissue resection of a fibrosarcoma of the deltoid muscle already described.

be considered per se an indictment of the treatment method employed. It is not anticipated that a better over-all salvage in sarcomas of soft parts will be accomplished by extensive resection of soft tissue than by primary amputation, but, if wisely employed, this method should offer a salvage equal to that obtained by amputation. While function of the extremity may be somewhat impaired following radical resection of soft tissue, particularly if an entire functional muscle group or its nerve supply is ablated, nevertheless, it is our belief that the patient's own extremity even if somewhat functionally impaired is preferable to an artificial limb.

Based upon experience with 37 patients* subjected to extensive resection of soft tissue for sarcoma the following points seem worthy of comment.

Histologic Type and Location.—Twenty-nine patients had sarcomas of the lower extremity and 8 of the upper extremity (Table I). There were 18 female and 19 male patients in this group varying in age from 1 month to 79 years. Rhabdomyosarcoma and liposarcoma occurred with equal frequency and were the most commonly encountered tumors (Table II).

TABLE I. ANATOMIC LOCATION OF RESECTION OF SOFT TISSUE FOR SARCOMA
(Memorial Cancer Center, New York)

	MALE	FEMALE	TOTAL
Arm	4	2	6
Forearm	–	2	2
Buttock	4	5	9
Thigh	10	6	16
Leg	1	3	4
Total	19	18	37

TABLE II. HISTOLOGIC TYPE OF RESECTION OF SOFT TISSUE FOR SARCOMA
(Memorial Cancer Center, New York)

	MALE	FEMALE	TOTAL
Rhabdomyosarcoma	5	6	11
Liposarcoma	7	4	11
Fibrosarcoma	4	2	6
Synovial sarcoma	2	2	4
Other	1	4	5
Total	19	18	37

Local Recurrence.—In 5 patients local recurrence of the sarcoma developed within 15 months, and, in one patient with a huge liposarcoma of the buttock, intrapelvic recurrence of the tumor was noted almost 7 years following apparent control of the primary. Whether this latter patient had true local recurrence or metastasis in deep pelvic nodes cannot be determined, but it is quite evident that the other 5 either were unwisely selected for resection of soft parts or were treated inexpertly by this method. Three of these locally recurrent tumors were rhabdomyosarcomas. One of these patients subsequently died with persisting disease, another had a high-thigh amputation for recurrence 13 months following resection of soft tissue but died subsequently of pulmonary metastases, and a third patient, a 3-year-old girl, had secondary amputation 8 months following local resection and remains living and free of disease

*Our associate, Dr. Joseph G. Fortner, has kindly permitted the inclusion of a personal case treated after the method just described.

3½ years following amputation. A fourth patient had local recurrence of a synovial sarcoma of the thigh and subsequently died of pulmonary metastases. A fifth patient had several recurrences of an extraosseous osteogenic sarcoma of the buttock and eventually died with persisting local disease and pulmonary metastases. Nine of the remaining patients have died of disseminated metastases although at no time did they show evidence of local recurrence. One patient is living with disseminated metastases from a primary liposarcoma of the thigh but remains free of local recurrence. One patient has not been seen since her return to Europe over a year ago but was free of local and metastatic cancer one year following radical resection of the anterior compartment of the thigh for rhabdomyosarcoma and 4 months following a right upper lobectomy for a solitary metastasis. The other 20 patients remain living and well from 2 to 7 years since undergoing extensive resection of soft tissue for sarcoma. Too few cases are available at present for conclusions based upon 5-year salvage figures.

Postoperative Function.—Nine of the 29 patients with sarcomas of the lower extremity had radical resection of the buttock, as has been described elsewhere.[2] In spite of sacrifice of the musculature of the buttock, none had significant disability. The 20 other patients with sarcoma of the lower extremity had varying slight degrees of disability, the most marked of which was caused by resection of the femoral nerve along with the rectus femoris muscle for liposarcoma. This patient cannot climb stairs easily but by virtue of adductor and iliopsoas function can walk on the level and perform household chores.

Of the 8 patients with sarcomas of the upper extremities, 2 patients sustained wrist-drop deformities and 3 patients had some limitation in abduction of the arm at the shoulder.

It has been quite gratifying to observe how well all of these patients have accommodated to their disability and how, in every instance, they successfully resumed their former occupations and activities within a short while following surgery.

SUMMARY

Sarcomas of soft parts are characterized by an absence of true encapsulation, by filamentous extension within muscle fasciculi and along contiguous fascial planes and nerve trunks well beyond visible and palpable tumor, and by occasional metastasis by way of lymphatics. Treatment in order to be locally successful, therefore, must be aggressive.

The thesis is offered that the gross anatomic setting of the sarcoma, and not its histologic type, should be the primary criterion in determining whether amputation or extensive resection of soft tissue be employed for accomplishing adequate treatment.

When resection of soft parts is anatomically feasible for the removal of a sarcoma, it includes wide ablation of surrounding grossly normal tissue, removal of entire muscle bundles at points of origin and insertion, employment of sharp dissection throughout, minimal handling and massage of the tumor and proximal ligation of major venous tributaries early in the procedure.

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ANASTOMOSIS OF THE BRANCHES OF THE FACIAL AND SPINAL ACCESSORY NERVES FOR FACIAL PARALYSIS

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IN THE recent surgical literature there have been numerous descriptions of the anatomy of the facial nerve and the parotid gland and the surgical approach to removal of tumors of the parotid. We cannot agree with these descriptions of the parotid gland as a bilobed structure with a connecting isthmus around which the branches of the facial nerve pass, nor do we believe that the nerve can be exposed "like opening the pages of a book." Our experience is in keeping with that of Lathrop[5] who states that such an anatomic description is a misconception and that the facial nerve penetrates the substance of the parotid gland and, thereafter, repeatedly divides in a fan-shaped manner on a sagittal plane until the branches emerge at the perimeter of the anterior border of the gland. Thus, the facial nerve, rather than running between two lobes of the gland, actually courses through the parotid gland and merely affords a plane of dissection which may be followed. With knowledge of this anatomy and with careful dissection, it is possible to remove all benign tumors of the parotid without damaging the nerve. However, no consideration of the cosmetic and functional results of facial paralysis should be allowed to compromise the chance of cure when dealing with a malignant tumor, and it may be necessary to sacrifice all or part of the nerve in making a wide bloc removal of the tumor.

Facial paralysis is a most distressing condition. It leaves a flat, expressionless, distorted face with atrophy of the musculature on the paralyzed side. There is constant epiphora and possibility of corneal ulceration, drooling of saliva, and difficulty in mastication. Possibly worse than the functional disability is the psychologic effect on the patient, sometimes making a recluse of an otherwise normal person. Martin[6] recently made the interesting observation that there was some spontaneous recovery in about one-fourth of his cases and postulates that motor pathways are re-established by way of the fifth cranial nerve. Intriguing as this possibility is, in the experience of most surgeons, facial paralysis due to destruction of the nerve is a serious and permanent disability.

Various methods have been used in attempting to correct or alleviate this condition. In general they fall into 4 categories: (1) support by fascial strips or metallic foreign material, (2) muscle transplant, (3) nerve graft, and (4) nerve transplant. The multiplicity of procedures and the innumerable variations in technique indicate the general dissatisfaction with results.

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The use of fascial supporting strips was popularized in this country by Blair.[1] Numerous attempts have been made to restore some motion by attaching the strips to the temporal or masseter muscles. All that can be accomplished by this method is to restore the symmetry of the face in repose. It can have no effect on the muscular atrophy and can restore no emotional expression. In practice there is usually overcorrection at first with gradual relaxation and undercorrection after a period of years.

Transplantation of slips of muscle from the temporal, masseter, or sternocleidomastoid sometimes supplemented by fascial strips has been described by Conway,[4] Gilles, McLaughlin, and others. These procedures result in some rehabilitation but should be reserved for those cases in which nerve graft or transplant is not applicable or has failed. Conway considers paralysis of more than one year's duration as not amenable to neurosurgical procedures.

Replacement of the excised portion of the facial nerve by free nerve graft has been described by Conley[3] and Lathrop. The posterior auricular nerve from the opposite side or the femoral cutaneous nerve has been used. Results have been excellent in some cases, but the percentage of failures has been high, as in all free nerve grafts. In 1955, Conley reported 7 cases in three of which there was good (60 to 90 per cent) return of function, one had a fair result (30 per cent return of function), and in three there was total failure.

The transplantation of the spinal accessory or the hypoglossal nerve to the severed trunk of the facial nerve has been reported many times with varying results. Usually there have been disturbing mass movements and movements associated with motion of the shoulder. In any case, this method is possible only when the facial nerve is damaged intracranially, as in mastoid or acoustic nerve surgery, or in intractable Bell's palsy, and is not applicable after removal of the main facial trunks in parotid surgery. Coleman,[2] in 1950, reported the first successful suture of the branches of the eleventh nerve to the peripheral branches of the facial nerve after the major portion of the nerve had been removed during an operation for parotid tumor. The result demonstrated by him was so successful that I was led to use it in two recent cases.

CASE REPORTS

CASE 1.—Mrs. L. A., age 32, presented a small movable tumor about 1.5 cm. in diameter in the lower anterior part of the parotid gland. It had been present about 8 months with slow increase in size. There was no pain or other symptoms.

On June 2, 1956, the parotid gland was exposed in the usual manner, and, since the tumor was low and somewhat anterior, the mandibular branch of the facial nerve was identified anteriorly and traced backward. It was anticipated that the lower part of the superficial lobe including the tumor could easily and quickly be removed. Instead, the nerve ran directly into a hard nonencapsulated tumor which appeared to be malignant and proved to be so on frozen section. The trunk of the facial nerve was identified over the styloid process and traced forward. Again the lower branches ran directly into the tumor. The lower two-thirds of the parotid gland with the tumor was removed. This necessitated shaving the tumor off the lower branches of the nerve. I was reluctant to sacrifice the nerve without benefit of paraffin sections; so the wound was closed.

Permanent sections confirmed the frozen section diagnosis, and, since this was obviously an inadequate operation, a total parotidectomy and radical neck dissection was performed one week later, sacrificing the facial nerve from the styloid process to the anterior border of the parotid gland at which point there were 4 main branches. The spinal accessory nerve was dissected out of the sternomastoid muscle and the branch to the trapezius was severed where it entered the muscle. The branch to the sternomastoid divided into 2 bundles in the muscle and these were easily separated proximally to make 3 nerve trunks. The 2 lower branches of the facial nerve were brought together and sutured to the largest branch of the spinal accessory. The 2 smaller branches were sutured to the smaller divisions of the spinal accessory. Simple through-and-through sutures of 6-0 silk were used. With the aid of a binocular loupe this was not difficult. Suction drainage was applied by means of polyethylene tubes brought out through a stab wound, and the wound closed. Healing was without incidence.

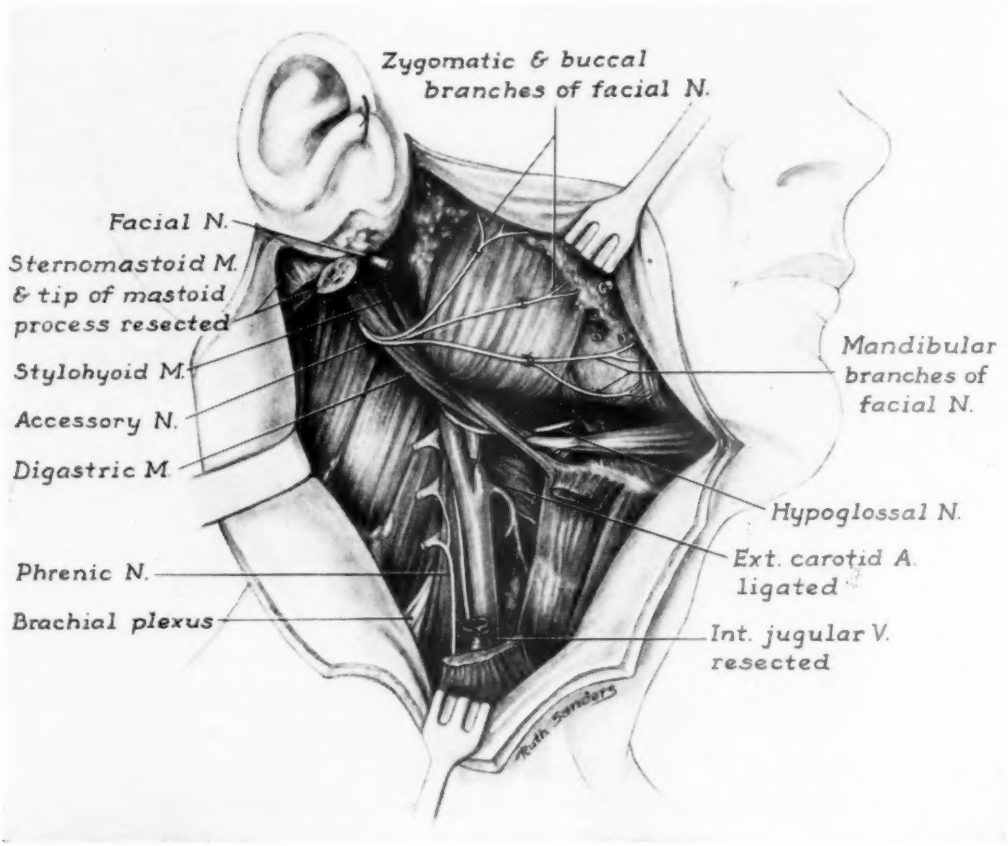

Fig. 1.—Spinal accessory nerve transplant to the peripheral branches of the facial nerve as performed in Case 1. In Case 2 a similar procedure was carried out except that the upper branch of the facial nerve was preserved and only the buccal and mandibular branches were sacrificed and replaced.

At 2 months there was definite beginning return of function. This steadily improved until at 8 months there was complete recovery of all muscles except part of the orbicularis oris in the lower lip. The face was symmetrical in repose, there was no atrophy, the eye could be completely closed, and there was considerable emotional expression. At first there was some involuntary twitching about the mouth, associated with motion of the shoulder, but at no time has there been any mass movements. The patient has not complained of any disability of the shoulder. She cannot abduct the arm directly laterally, but by bringing it slightly forward and up there is a full range of motion.

CASE 2.—Mrs. G. H., age 48, presented herself with a hard, painful tumor about 3 cm. in diameter located deep in the lower portion of the parotid in the jugular notch. There was no paralysis. At operation, on Jan. 21, 1957, frozen section confirmed the clinical impression of carcinoma. A total parotidectomy and radical neck dissection were performed sacrificing all the facial nerve except the zygomatic branch. This was well above the tumor, and it was felt it could be preserved without compromising the chance of cure. The branches of the spinal accessory nerve to the sternomastoid and trapezius were anastomosed to the buccal and mandibular branches of the facial nerve. At the end of 2 months there was beginning return of function and at 6 months complete recovery. It was interesting that postoperatively there was complete paralysis of the muscles supplied by the zygomatic branch due to the trauma and traction of its dissection. Recovery of the upper and lower facial musculature was practically synchronous.

Fig. 2.

Fig. 3.

Fig. 2.—Case 1. Photograph taken 22 months after removal of the left facial nerve and transplantation of spinal accessory to the peripheral branches.

Fig. 3.—Case 2. Fifteen months after total right parotidectomy with sacrifice of buccal and mandibular branches of the facial nerve and replacement by 2 branches of the spinal accessory.

DISCUSSION

When it is necessary to sacrifice the facial nerve in removing a parotid tumor, an attempt should be made to restore facial function by neurosurgical methods. The many and ingenious attempts to restore symmetry and motion by fascial slings and/or muscle transplants are at best palliative and leave

much to be desired. Whether the neurosurgical approach should be free nerve graft or a free nerve transplant is unsettled and must await the accumulation of more cases.

It has been objected that the use of the eleventh nerve transplant violates the principle of en bloc removal in cancer surgery. I do not believe that this is a valid objection, for, if the spinal accessory nerve is involved in tumor or even closely associated with it, a curative procedure is hardly possible. This is attested to by the fact that some surgeons preserve the sternomastoid muscle itself when doing a radical neck dissection. Another objection is the disability of the shoulder caused by paralysis of the trapezius. Coleman showed that the trapezius receives varying portions of its innervation from the cervical plexus and the disability caused by transplant of the spinal accessory was not significant in his case as it was not in the 2 cases here reported.

One objection to the free graft technique is that if you double the number of anastomoses, as you do in a free graft, you double the chance of failure, for failure always occurs at the suture line. Conley's report of 50 per cent failure is not reassuring. It is probable that troublesome mass movements will be more common with a graft from the trunk of the facial nerve to its peripheral branches. Mass movements are probably caused by nerve fibrils straying when growing downward into different peripheral branches. Another theory is that there is failure of maturation at the suture line and there is cross stimulation when impulses pass across an anastomosis. In either case there will be more likelihood of mass movements when the trunk of the facial nerve is anastomosed to a graft. In fact, when the trunk of the facial nerve is simply divided and resutured, there is great likelihood of mass movement and loss of coordinated emotional expression.

Another objection to the graft technique is the length of time required for restoration of function, if it occurs. In Conley's series the earliest beginning of recovery was 8 months. In contrast, in Coleman's case and the two reported here, there was evidence of recovery in 2 months. This is of tremendous psychologic importance to the patient. The first muscular twitching of returning function gives the morale a tremendous boost. In addition, paralysis of 8 to 12 months may allow atrophy and fibrosis to such an extent that the final result will be impaired.

SUMMARY

Two cases are presented illustrating good recovery with little shoulder disability after anastomosis of the branches of the spinal accessory nerve to the peripheral branches of the facial nerve. No mass movements occurred. The success of these 2 cases and of Coleman's indicate that it should be given further trial to determine whether it is superior to free nerve graft. In any case, when the facial nerve is sacrificed, an attempt should be made to restore neuromuscular function. Spontaneous recovery is negligible and plastic procedures only ameliorate this distressing disability.

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A SIMPLE TECHNIQUE FOR ENDARTERECTOMY

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THE excision of thickened, ulcerated, and partially calcified intima with the thrombotic debris often accompanying it must be smoothly and completely executed without disruption of the remaining arterial wall if postoperative hemorrhage and thrombosis is to be avoided. Intimal dissection under direct vision has the disadvantages of a long suture line for reconstruction of the medial and adventitial sheath, suture line leaks, and significant luminal narrowing following closure of the long arteriotomy, particularly in the femoral artery. Closed loops of wire of different sizes have been recommended for removing the arterial occluding mass without opening the entire length of the occluded part of the artery.[1] Our attempts to remove obstructions within arterial segments with closed wire loops of varied designs and sizes have not been satisfactory. The dissection of an intimal core with closed wire loops frequently requires changing the loop during the endarterectomy: from a smaller to a larger when proceeding toward the heart and vice versa when proceeding toward the extremities. When changing from a smaller to a larger loop, the larger loop must be passed through the arteriotomy into a part of the artery which is often too small easily to receive it, occasionally tearing the medial and adventitial sheaths. When changing from the larger to the smaller loop difficulty in passing the large end of the core through the loop is experienced and the core may be broken and a piece of it left behind. In order to minimize these troubles during endarterectomies performed with closed wire loops, multiple arteriotomies were required. Fewer arteriotomies are needed to remove an arterial obstruction with a simple open bent wire loop than are needed for its removal with a closed wire loop. The technique of using the open bent wire is described.

TECHNIQUE

A stainless steel wire (gauge No. 18 or 20) approximately 30 inches long is bent upon itself and the open loop adjusted by bending to the desired size with sterile pliers (Fig. 1). The trailing ends of the wire remain apart and are bent approximately 30 degrees just behind the loop. First, the diseased intima is separated from the medial sheath with a dural elevator through a linear arteriotomy made just distal to the obstruction. Then the freed intima is transected and its distal free edge is sutured to the medial sheath with interrupted 5-0

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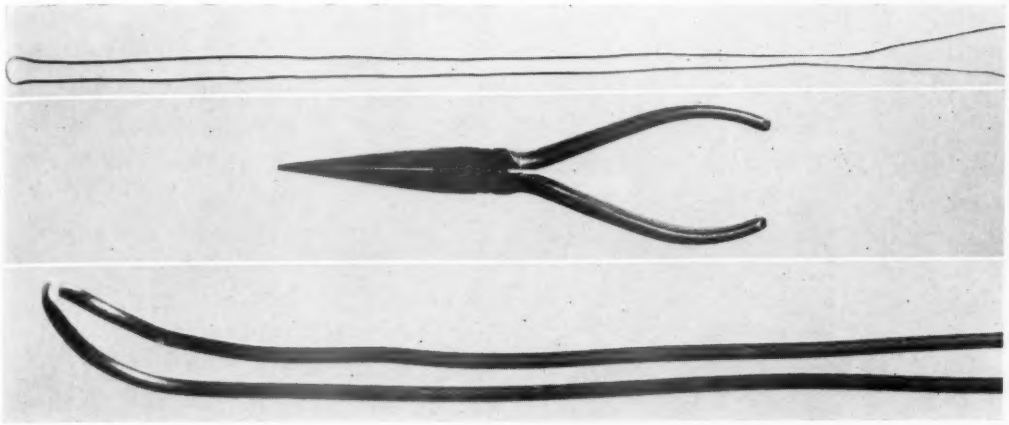

Fig. 1.—The open bent wire loop and pliers used for endarterectomy are shown above. The trailing ends are bent approximately 30 degrees just behind the loop as illustrated below.

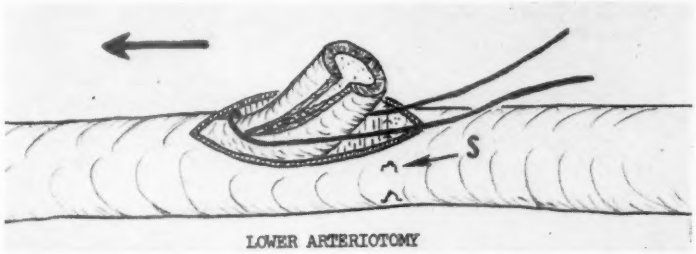

Fig. 2.—After dissecting and cutting the intima distal to the luminal occlusion and suturing its distal edge to the medial sheath under direct vision (at *S*), the wire loop is inserted into the cleavage plane between the intima and media and pushed proximally while counter traction is maintained upon the occluding core.

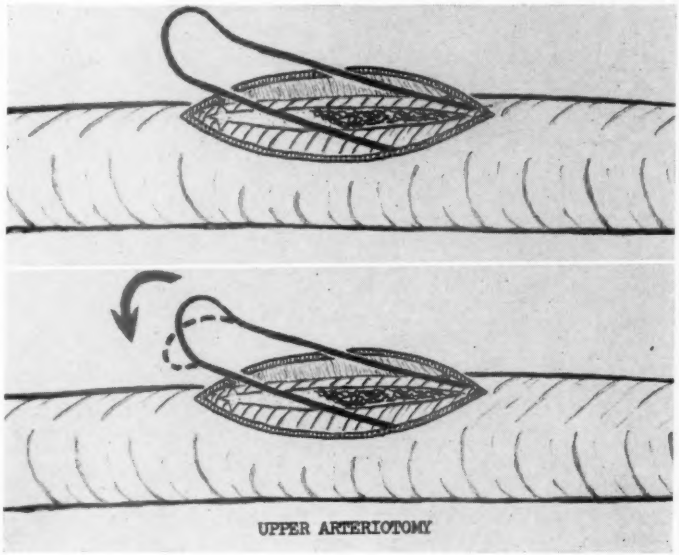

Fig. 3.—The wire loop has dissected approximately one-third of the circumference of the arterial wall from the occluding intimal core and presents through an arteriotomy made proximal to the occlusion (*above*). The trailing ends of the wire just behind the loop are rebent as diagrammed by the dotted line (*below*).

arterial silk to prevent the subsequent dissection of the intima from the media by flowing blood. After this, the intima is freed proximally for 1 to 2 cm. under direct vision. The wire loop then is inserted into the plane of cleavage developed and the freed intima is grasped firmly below the wire loop (Fig. 2). The wire loop is passed gently along the vessel wall dissecting intima from media through

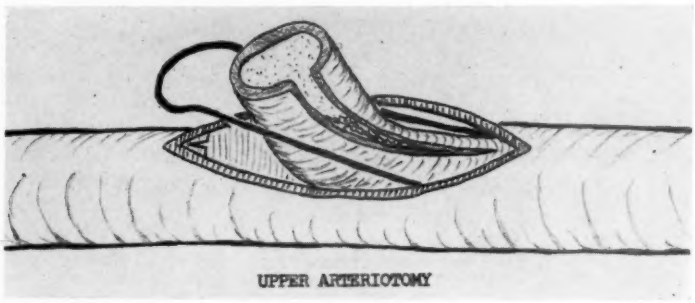

Fig. 4.—The proximal end of the intimal core has been dissected free under direct vision and severed. After the angulation near the end of the wire loop has been reversed, the intima to be removed is passed through the loop.

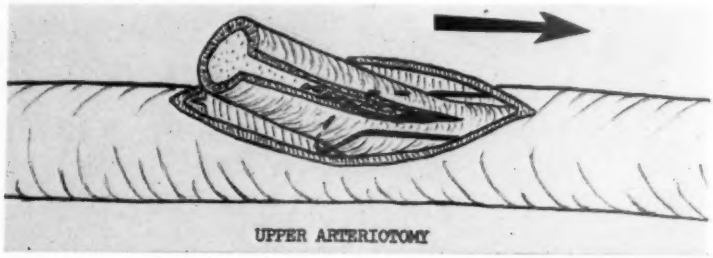

Fig. 5.—Withdrawal of the wire loop is begun. Gentle traction must be applied to the intimal core in the proximal direction during withdrawal of the wire loop.

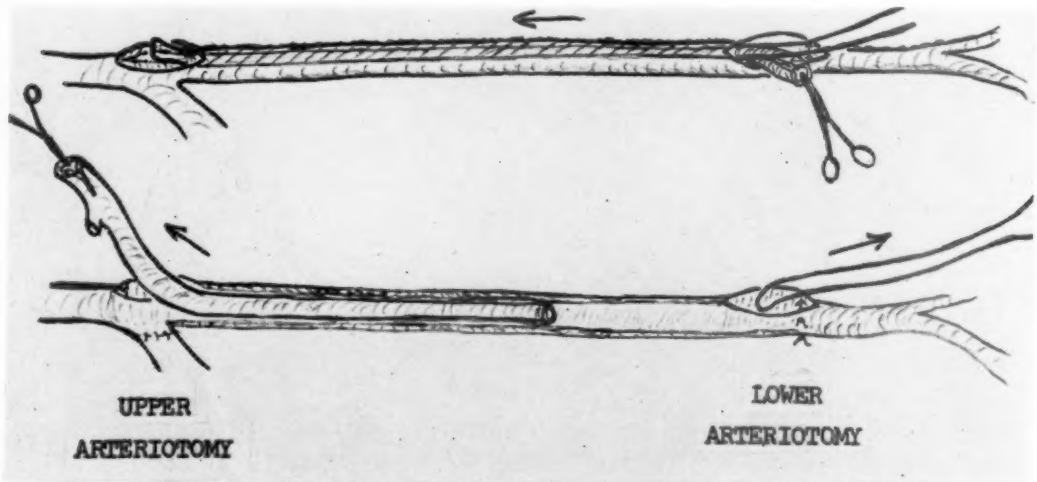

Fig. 6.—*Above*, The occluding core has been partially dissected by passage of the wire loop from the lower to the upper arteriotomy. *Below*, The intimal dissection has been completed by withdrawal of the wire loop. The diseased intima is removed as a single specimen through the upper arteriotomy. The dissection is best begun below because of the danger of tearing the medial sheath with a loop too large to continue down the smaller distal artery.

one-third to one-half the arterial circumference to a point above the luminal occlusion. At this point the previously exposed proximal part of the artery is opened longitudinally over the end of the wire loop (Fig. 3), and the remaining circumferential attachment of the intima is freed from the media with the dural elevator and served proximally (Fig. 4). The looped end of the wire is then passed through the upper arteriotomy and the loop rebent so that the transected end of the core can be brought through it while the position of the trailing wires is maintained (Figs. 3 and 4). The proximal freed end of the intimal core is firmly grasped *through* the open loop. The remaining circumferential attachment of the intimal core is then severed by gently withdrawing the wire loop toward the lower arteriotomy (Fig. 5). Subsequently, the occluding core may be withdrawn in toto through the upper arteriotomy incision after the wire loop has been withdrawn through the lower one (Fig. 6).

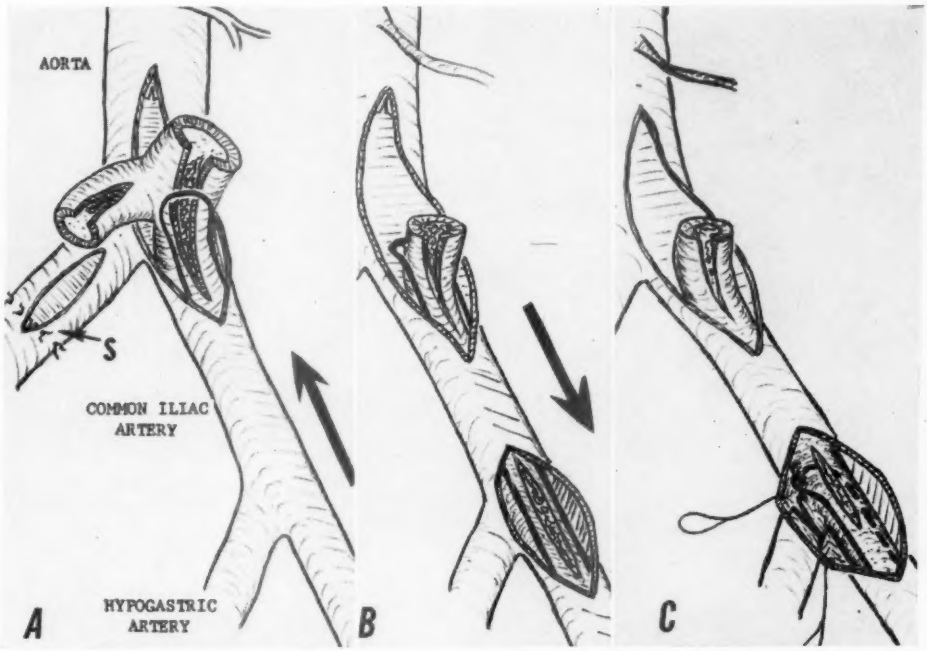

Fig. 7.—The drawing (*A*) shows the wire loop (introduced from an unseen distal arteriotomy in the left ileofemoral system) presenting through an arteriotomy at the aortic bifurcation. Dissection of diseased intima at this point has been accomplished under direct vision; the transected intima in the right iliac artery has been sutured to the medial wall (*S*). The drawing (*B*) shows the beginning withdrawal of the wire loop. Before the loop dissection is completed however, the intimal branch into the hypogastric artery is cut under direct vision (*C*) to avoid tearing the occluding core and to prevent occlusion of a possibly patent hypogastric artery.

This technique has been used to remove the diseased intima of the entire external femoral and upper popliteal artery, the common femoral and external iliac arteries, the common iliac artery, and the abdominal aorta. If the free ends of the wire are long, the open loop can easily be passed many inches proximally. The insertion of the flexible wire is little hindered by branching cores of occlusive disease. The convex loop usually slides to the side of such a branch. The smaller branches are severed easily during withdrawal of the loop. However, one should

not attempt blind endarterectomy at points of major arterial bifurcation such as those of the common iliac and common femoral arteries because of the danger of occluding important pathways of blood flow such as the hypogastric and deep femoral arteries. In addition, the attempted transection of such large branches of the intimal core with the wire loop is likely to break the core and lead to its incomplete removal. However, the wire loop may be used to remove an obstruction from the external or common iliac arteries. It is passed easily through a common femoral arteriotomy up to the aortic bifurcation anteriorly (Fig. 7, A);

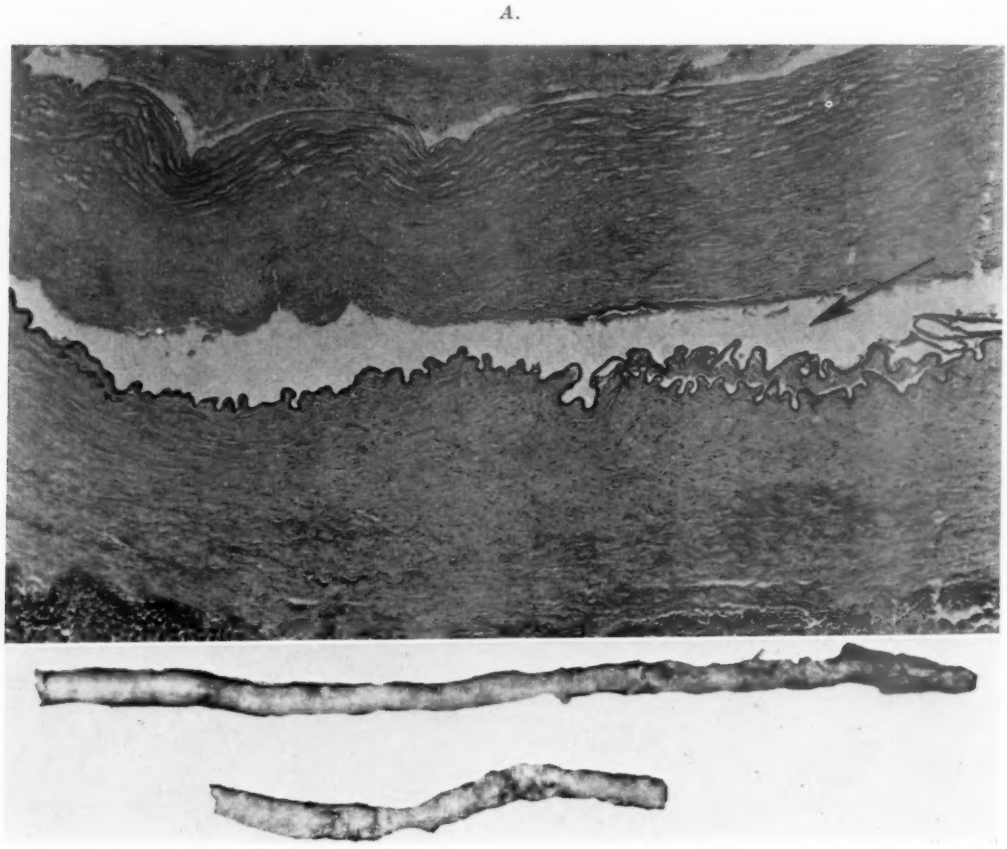

Fig. 8.—*Above*, Photomicrograph of an occluded artery subjected to wire loop endarterectomy. Tissue sections were made with the dissected intimal core left in situ. Note the uniform plane of cleavage at the internal elastic lamina (arrow). *Below*, Photograph of an ileofemoral intimal core 30 cm. in length. It was removed intact after being freed from the medial sheath with an open bent wire.

upon withdrawing the rebent loop, another arteriotomy made overlying the origin of the hypogastric artery and the wire is withdrawn until it impinges upon the hypogastric intima (Fig. 7, B). The intimal branch into the hypogastric artery is then transected by sharp dissection under direct vision (Fig. 7, C), and the wire dissection of the posterior intimal attachment in the external iliac and common femoral arteries is subsequently completed by finishing the withdrawal of the open loop.

The advantages of this method of endarterectomy may be summarized as follows:

1. No specially designed instruments are required.

2. The open loop of steel wire is in part adaptable to moderate changes in arterial size because of its flexibility.

3. The method is easily and rapidly executed; it minimizes discontinuous irregular intimal dissection and the number of arteriotomy incisions. The uniform cleavage plane developed by the wire loop is illustrated in Fig. 8, A. Intact specimens 30 cm. long have been removed using this method of intimal dissection (Fig. 8, B).

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A NEW METHOD OF ARTERY GRAFT ANASTOMOSIS

An Experimental Study

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THE purpose of this paper is to describe an artery graft anastomosis applicable to a bypass procedure which approximates the intraluminal orifice profile of arteries that originate from the aorta and its pelvic branches.

METHOD OF INVESTIGATION

Ten abdominal aortas, including the pelvic branches, were removed and studied during routine postmortem examination. The specimens were divided in their longitudinal axis, and the renal, celiac, common iliac, and external iliac artery orifices were examined, and the following noted: (a) the intraluminal orifices of branched arteries originating from the aorta were, in most instances, conical in design with the posterior wall being concave, smooth, and somewhat V-shaped in appearance; (b) the anterior wall, however, presented a well-defined, sharp ridge that projected into the lumen of the aorta for varying distances, but seldom over 2 mm. (Fig. 1).

In an effort to reproduce these orifices by a surgical technique the following method was developed (Figs. 2 and 3). A flap of full thickness artery wall was made with the apex of the flap wider than its base and the flap rotated 180 degrees in the direction of the long axis of the host artery. A suitable artery graft was prepared by tailoring the open end of the artery graft to fit the created trap-door orifice. The anastomosis was completed by the Carrel suture technique, using 5-0 arterial silk suture.

This procedure was employed in 10 adult mongrel dogs weighing 15 to 17 Kg. In each instance, an 8 cm. freeze-dried preserved artery homograft was anastomosed to the abdominal aorta by the method described. The distal anastomosis was fashioned by the conventional end-to-side method to the common iliac artery above the origin of the hypogastric artery. Once blood flow was established, the common iliac artery was ligated so that in essence the graft simulated an arterial bypass procedure.

A comparison study employing a similar number of animals was made; however, the artery bypass procedure was constructed by an end-to-side fashion as described by Linton.[1] All animals were sacrificed at the end of 30 days, at which time 5 of the 10 grafts in which the trap-door type of anastomosis was made were found patent. Of the 10 grafts in which the conventional type of end-to-side anastomosis was employed only 2 were patent (Fig. 4).

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Fig. 1.—The photograph shows the conical design of the external iliac artery orifice. Note the sharp projecting ridge of the anterior wall and the V-shaped appearance of the posterior wall.

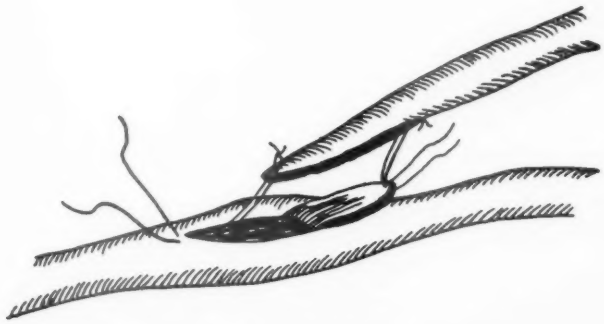
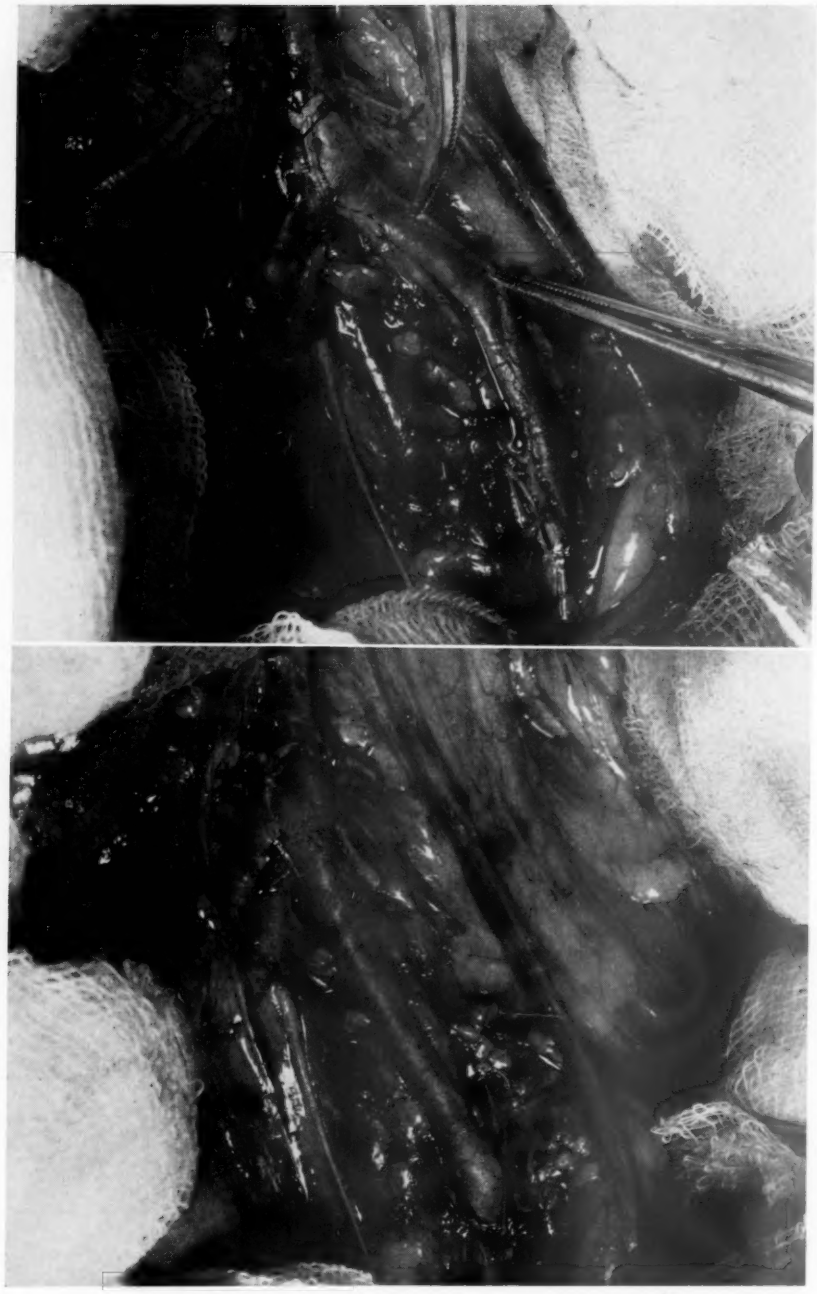


Fig. 2.—Artist's conception of the technique employed in creating a so-called "trap-door" artery graft anastomosis.

Fig. 3.—A completed "trap-door" artery graft anastomosis. Note the similarity to the normal orifice of the common iliac artery.

A.



B.

Fig. 4.—*A*, Photograph showing a "trap-door" graft anastomosis in an experimental animal. A portion of the artery flap and the anastomosis is shown adjacent to the tip of the curved hemostat. *B*, Appearance of the artery graft following establishment of blood flow.

DISCUSSION

The observations described herein concerning the anatomic profiles of arteries originating from the aorta suggest a dual purpose. First, the conical design of the artery orifices adheres to well-established hydraulic principles, namely, a smooth, well-rounded orifice between pipes of different diameters insures the most effective flow system. If these orifices were constructed in any other fashion, factors would be introduced that would favor turbulent flow pattern, the effect of which would lead to decrease in the efficiency of the flow system. In addition, turbulent blood flow, when present in the human vascular tree, has been suggested to be a factor in the production of intravascular thrombi.[2] Second, the presence of the sharp anterior ridge projecting into the lumen of the aorta behaves in a similar fashion, namely, by interfering with the laminar pattern of the aortic blood flow in the most minimal degree possible. Furthermore, most surgical procedures are so designed to simulate, as near as possible, the normal anatomic architecture. The formation of a "trap-door" end-to-side artery anastomosis fulfills, in part, the anatomic features of an artery orifice whose origin is from the aorta or its major branches.

SUMMARY

A new method of artery graft anastomosis has been presented. Its prinicpal features are: (a) it resembles in part the orifice of an artery originating from the aorta, and (b) in experimental animal studies a slight but significant number of patent grafts were obtained when compared with the conventional end-to-side technique.

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A NEW TYPE OF ARTERIAL PROSTHESIS

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NUMEROUS materials and fabrications have been studied in the search for a satisfactory arterial prosthesis.[1] Many have been tried and discarded, and despite some successes the synthetic graft which fulfills all requirements still remains to be described. Experimental data concerning a new type of nylon prosthesis are reported in the present paper. This is of novel design and offers in particular a solution to the problem of flexibility. Messrs. P. Davenport Ltd. are responsible for both its design and manufacture.† That nylon is not the most suitable material for a prosthesis will be discussed later; however, other fibers may as readily be used. Synthetic grafts of this design have been inserted in the arterial trees of dogs and studied in general at least 30 weeks later.

GRAFT MATERIAL

The flexibility and noncollapsibility of this prosthesis are achieved by using the principle of a coil spring (Figs. 1 and 2). The weft consists of continuous alternating spirals of a fine multifilament thread and heavy monofilament with an overbraid. The warp is of multifilament yarn. The purpose of the overbraid on the heavy monofilament is twofold, to prevent sideslip of the warp on the monofilament which might lead to the appearance of small holes in the tube and to help fill the interstices of the weave immediately above and below the monofilament. The tube may be made of any length and caliber and produced with a taper if necessary. The specifications of the weave are as follows. The thick nylon monofilament is 0.015 inch in diameter braided over with 16 ends of 100 denier nylon; the other weft is one end of 100 denier nylon. There are 19 rings of monofilament with 19 spacing rings per inch giving 76 picks per inch. The 4.7, 5.5, 6.7, and 8.3 mm. internal diameter tubes have 128, 144, 180, and 224 warp ends of 100 denier nylon, respectively. After weaving it is "ironed" on a hot metal rod, but no chemical treatment is given to the tube. Readily autoclaved, it may be siliconed if thought desirable. This prosthesis holds sutures well but it is necessary to seal the ends prior to use to prevent ravelling; this is easily performed by dividing the tube with the cautery.

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*Histologic observations by Dr. Curran.

†This has been registered as a patent process by Messrs. P. Davenport Ltd., Bridge Street Mills, Macclesfield, Cheshire, England.

EXPERIMENTAL PROCEDURE

Healthy dogs of both sexes (15 to 26 Kg. in weight) were used; they were premedicated with morphine 3 mg. per kilogram subcutaneously and anesthetized with intravenous Dial:Urethane* and Veterinary Nembutal† (50:50). An intravenous glucose-saline transfusion was set up and full aseptic technique was followed. The ends of the receiving arteries controlled with tapes or rubber-shod Crile clamps were washed with normal saline. In all cases end-to-end anastomosis was carried out with 4-0 or 5-0 arterial sutures using everting mattress or simple through-and-through sutures. No "preclotting" was used with any of the grafts. The host vessel was not pulled over the graft but sutured in direct apposition. Only one prosthesis was inserted into any one dog. The animals were not heparinized and no special postoperative treatment was given, although one-half mega unit of soluble penicillin was injected intramuscularly immediately prior to operation.

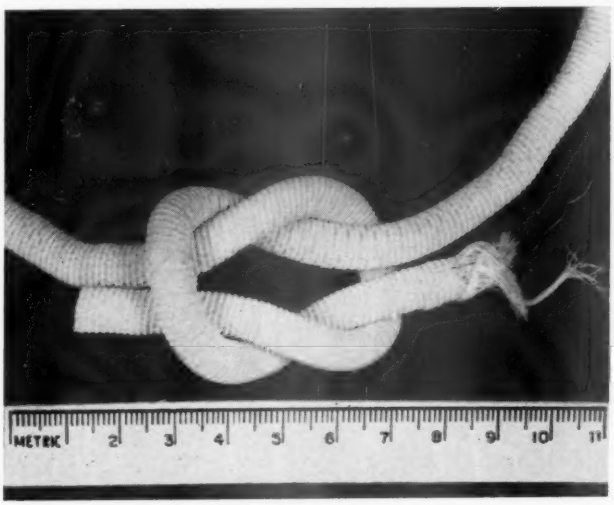

Fig. 1.

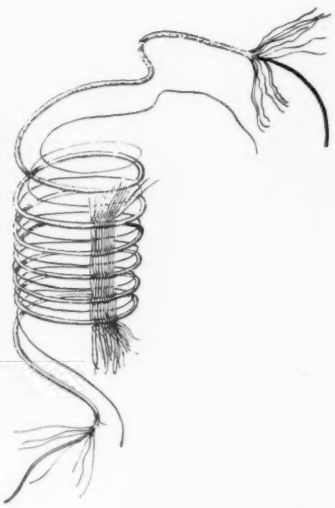

Fig. 2.

Fig. 1.—A prosthesis knotted to demonstrate its flexibility. The constituent fibers can be seen at one end; the other has been sealed ready for use.
Fig. 2.—A drawing of the graft expanded to show its mode of weaving.

Three sites (Table I) were chosen to receive the grafts: (1) the abdominal aorta just above the trifurcation, (2) the external iliac artery, and (3) the iliofemoral artery.

1. The *aorta* was approached transabdominally through a paramedian incision. Four grafts of 8.3 mm. and one of 6.7 mm. internal diameter were inserted. One dog failed to recover from the anesthetic and was found at autopsy to have massive pulmonary collapse; another died one week after operation with a ruptured abdomen. The rest of the animals remained healthy and were sacrificed at 31, 32, and 33 weeks, respectively, after operation.

*Supplies of Dial:Urethane were generously provided by Dr. J. A. Munro, of Ciba Ltd.
†Abbott Laboratories Ltd.

2. The *iliac artery* approach was similar to that of the aorta; two grafts were inserted, one of 5.5 mm. and one of 4.7 mm. internal diameter. These animals remained fit and well to be sacrificed 32 and 36 weeks, respectively, after operation.

3. The *iliofemoral* insertion was made using two incisions, one a pararectal type to expose the iliac artery transperitoneally in the iliac fossa, and the other over the femoral vessels centered 3 cm. distal to the inguinal ligament. A channel under the ligament was made lateral to the artery and a glass tube was threaded into the retroperitoneal tissues. This channel often ran in the psoas muscle sheath. A graft of suitable caliber and appropriate length was slid down the glass tube and the latter was withdrawn to leave the graft in place. Care was taken, especially in the femoral wound, to reconstitute all the anatomic layers.

TABLE I. NYLON DAVENPORT GRAFTS

DOG NUMBER	WEIGHT (KG.)	INTERNAL DIAMETER (MM.)	LENGTH OF GRAFT (CM.)	SITE OF ARTERY	TIME OF INSERTION (WEEKS)	PATENCY	RUPTURE LOAD (LBS.)	REMARKS
1	17.0	8.3	2.5	Aorta	31	Yes	–	Sacrificed
2	19.5	8.3	3.0	Aorta	32	Yes	–	Sacrificed
3	21.5	8.3	2.0	Aorta	33	Yes	–	Sacrificed
4	26.0	8.3	2.5	Aorta	1	Yes	–	Died
5	20.0	7	2.5	Aorta	1 day	Yes	–	Died
6	20.5	5.5	4.0	Iliac	32	No	–	Sacrificed
7	18.0	4.7	4.0	Iliac	36	No	–	Sacrificed
8	24.0	5.5	9.0	Iliofemoral	31	No	–	Sacrificed
9	22.0	4.7	10.0	Iliofemoral	33	No	3½	Sacrificed
10	20.5	4.7	10.0	Iliofemoral	35	Yes	9½	Sacrificed
11	15.5	4.7	11.0	Iliofemoral	34	No	7	Sacrificed
12	16.0	4.7	9.5	Iliofemoral	35	No	12½	Sacrificed
13 S	24.5	4.7	9.5	Iliofemoral	35	No	9½	Sacrificed
14 S	20.0	4.7	8.0	Iliofemoral	35	No	20½	Sacrificed
15 S	26.0	4.7	9.5	Iliofemoral	36	Yes	12½	Sacrificed

S = Siliconed.
On the average, the rupture load of unused 4.7 mm. prostheses was 44 pounds.

Seven dogs had iliofemoral segments replaced by grafts; two became septic and are omitted from further discussion. Four of the 5 dogs to be studied had 4.7 mm. internal diameter grafts; the remaining one was of 5.5 mm. internal diameter. Three other dogs had siliconed nylon grafts* of 4.7 mm. internal diameter inserted. All 8 of these animals remained healthy and were sacrificed between 31 and 36 weeks later.

Sacrifice.—The dogs were sacrificed at the intervals indicated previously. They were given subcutaneous morphine again before being anesthetized with intravenous Nembutal; 15 to 20 ml. of 30 per cent potassium oxalate was injected intravenously to cause cardiac arrest and at the same time act as an anticoagulant.

All those animals sacrificed had aortograms performed immediately post mortem. A polythene cannula was tied into the aorta immediately below the renal vessels. Fifteen per cent sodium iodide (12 to 15 ml.) was used as contrast agent.

*Grafts were siliconed with "Midland Silicones" solution 148 and catalyst N16.

OBSERVATIONS

Operative.—After exposure of the site the length of graft to be inserted was measured and cut from the autoclaved prosthesis with the cautery. This sealed the nylon tube most satisfactorily; division with scissors and attempts to seal the ends in a flame often caused charring of the nylon. Occasionally a fairly rigid nylon ring was produced as a result of the cautery division but this ring could be "cracked" by squeezing the area between the fingers. The pliability of the end was thus increased and suturing was made easier. The graft is, of course, considerably firmer than the natural artery but holds sutures extremely well. No case of "cutting-out" occurred.

Fig. 3.—Aortogram with patent nylon graft in situ.

On completion of the anastomoses, the distal occlusion was first released, followed by the proximal one 2 or 3 minutes later. At this time bleeding from the graft was free and intermittent occlusion of the host vessels had to be restored while the graft was packed tightly around with gauze. The prostheses were never "dry" in less than 3 minutes and four were generally required. Bleeding from the suture line was not a problem. The 3 siliconed grafts bled no less readily. Secondary hemorrhage did not occur, even in the two animals whose wounds became septic.

Survival.—The animals made very satisfactory recoveries and were walking about their cages the day following operation. They suffered no limitation

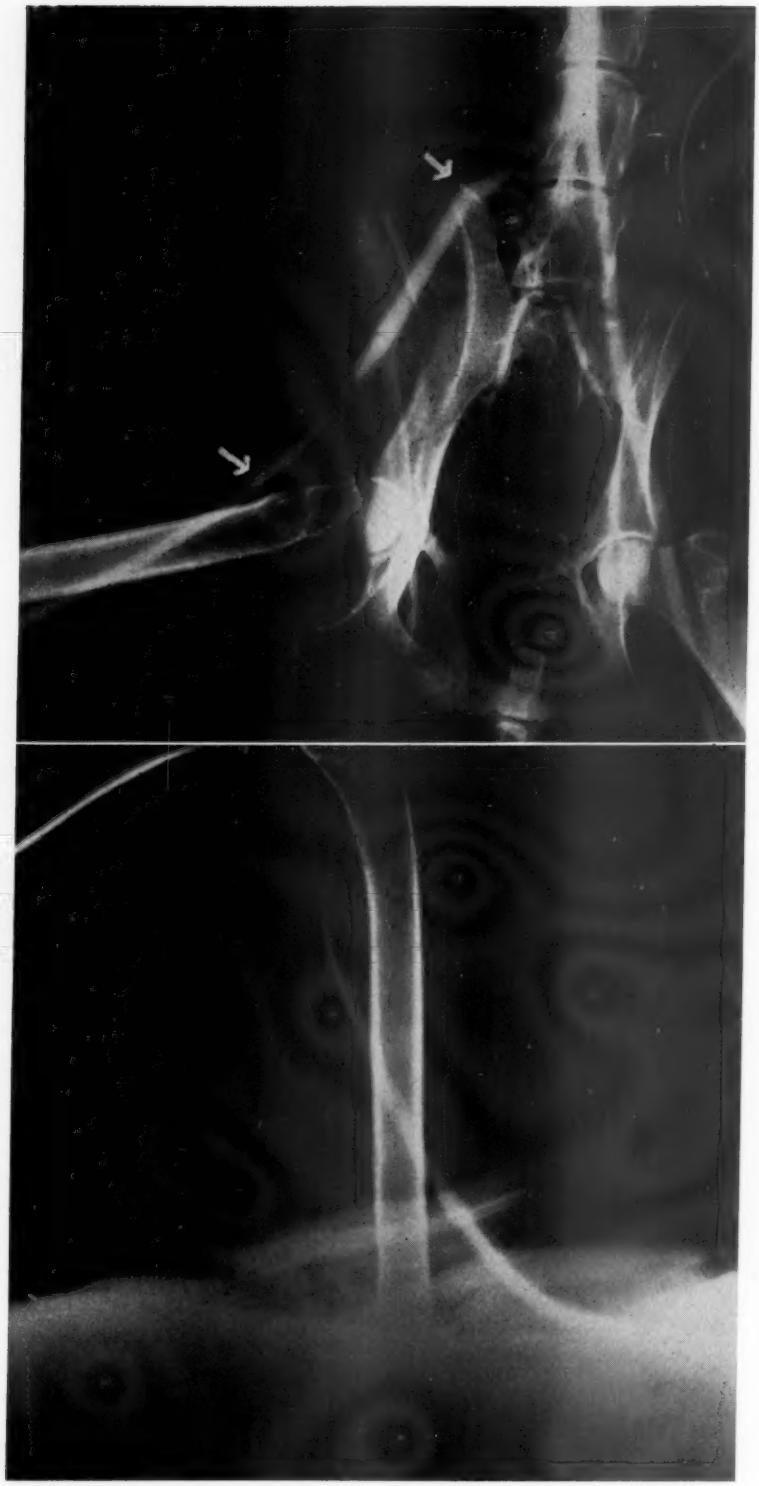

Fig. 4.—Arteriograms of a patent iliofemoral prosthesis. *A*, The anteroposterior position. *B*, Lateral view with the leg flexed at right angles to the body.

in their activities. Those with iliofemoral grafts which could be readily palpated under the skin were as active as normal dogs and displayed no disability.

Patency.— All the aortic grafts remained patent (Fig. 3). The other sites were disappointing however. Both iliac grafts clotted. Of the 5 nonsiliconed iliofemoral grafts, only one remained patent. One further siliconed iliofemoral graft of 3 inserted remained open (Fig. 4). The grafts that became occluded were blocked within 4 weeks of insertion. This was not associated with any disability of the animals.

Fig. 5.—A patent iliofemoral graft lying behind the inguinal ligament. Incorporation with the tissues is complete.

Autopsy.—Full autopsy of the animals was performed; none revealed evidence of disease relative to the experiment. However, one aortic graft, although it remained patent, was surrounded by an unorganized hematoma, and some light adhesions were found in relationship to the iliac and iliofemoral grafts. In most cases the graft could be seen shining through the peritoneum and in no case was there any evidence of thrombosis in collateral vessels which in the femoral region were sometimes lying in contact with the graft. Incorporation with surrounding tissues was complete (Fig. 5). There was no excessive fibrosis or evidence of irritation of the host tissues by the graft. The iliofemoral grafts lying under the inguinal ligament, whether thrombosed or patent, behaved as a normal artery when the animal's leg was flexed. This is well seen in the arteriograms of Dog 15S (Fig. 4) where kinking is absent when the limb lies in its normal flexed position. Slight irregularity of the new intima was seen in all arteriograms of animals with patent grafts; thus even after 30 weeks new tissue had not completely smoothed the luminal aspect of the graft, an event which might be thought likely to give rise to mural thrombosis. There was, however, no evidence of this or that emboli had arisen from the graft.

Strength and Flexibility.—In order to study the effects of contact with body fluids in regard to any loss of strength, unused and used portions of 7 of the 8 iliofemoral grafts, that is, those of 4.7 mm. internal diameter, were loaded to the point of rupture (Table I). Loading was carried out by taking the middle 5 cm. of the prosthesis, clamping one end between two steel bars in a vice and supporting a weight-holding platform of 24 ounces with the other end. One pound weights were added successively until the graft ruptured (failure of the warp). The segments chosen always included that length of graft which lay under the inguinal ligament since it was thought that this length was most likely to reveal the development of flexion fatigue in the material apart from the possibility of any chemical deterioration. The site of rupture, however, in the pieces tested occurred anywhere along their length and bore no relationship to that part which had been immediately behind the ligament. The average strength of the prosthesis after insertion was 24 per cent of the original material (76 per cent loss of strength). Possible weakening of the weft was not tested.

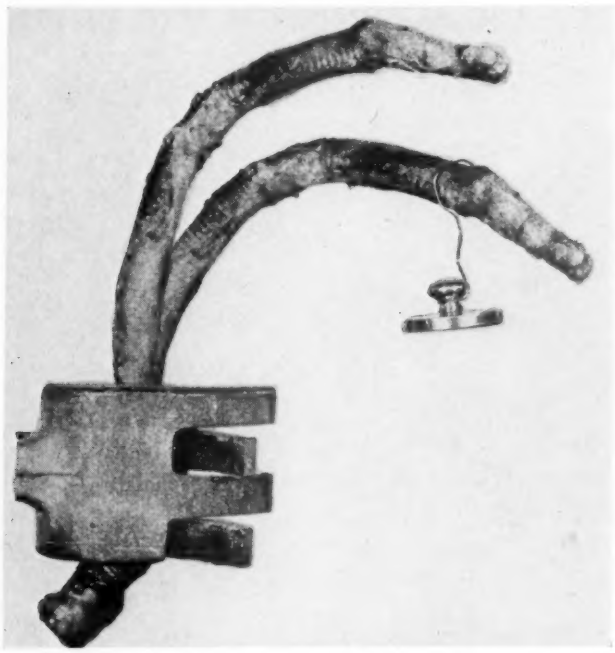

Fig. 6.—Flexibility of an excised patent iliofemoral prosthesis before and after loading with a 5 Gm. weight.

The longitudinal flexibility of the unused material is similar to that of a dissected artery. After insertion the prosthesis was considerably less flexible, but, nevertheless, pliability was still notable, as loading a patent segment 9.5 cm. long with a 5 Gm. weight shows (Fig. 6). Even when the graft was obstructed, pliability seemed to be very similar to that of the unobstructed. At autopsy when the skin had been removed and the animal's leg was flexed, there was no lack of response by the prosthesis to movement and muscles were not displaced or distorted as the limb moved.

Histology.—All grafts were in whole or in part referred for histologic study and this is described separately by Dr. R. C. Curran at the end of this paper.

DISCUSSION

Edwards[2] has discussed in detail the desirable properties of a synthetic vascular prosthesis. The tendency of woven, braided, or knitted tubes to collapse and kink when flexed was an unsolved problem until Edwards and Tapp[3] formulated their crimped nylon prosthesis. The Davenport nylon prosthesis relies for its flexibility and noncollapsibility upon the nature of its weave, properties not lost when incorporation in the tissues has occurred. Should it be desired to perform an end-to-side anastomosis, flexibility is sufficient to mould the graft to the receiving artery.

Suturing of the prosthesis has proved very satisfactory. The large monofilament and tightly woven warp permit sutures to gain a very powerful hold on the material. It is unnecessary—indeed, it is quite impossible—to cuff the tube.

The graft is not quite as smooth as those of conventional weave. Slight irregularity, as has been discussed by Edwards,[2] may have some advantage in anchoring the early lining of the graft. Nevertheless, it is surprising that after 30 weeks the new intima is not entirely free from the fine spiral depressions which follow the fabric's weave.

The porosity of the present prosthesis is too great, however, and siliconing failed to reduce its bleeding tendency to any extent. The porosity will be considerably reduced by increasing the number of warp ends in any graft so that a tighter fabric results. Preclotting should then seal the prosthesis completely.

The high thrombosis rate in the iliofemoral implantations may be attributable in some degree to this excessive porosity since much soft clot is extremely likely to accumulate in the narrow graft when bleeding necessitates repeated temporary clamping until the fabric has sealed. Nevertheless the small caliber of the arteries grafted in the iliofemoral region is likely to be a potent factor in militating against the persistence of patency. The iliofemoral site has not been sufficiently utilized in grafting experiments for comparisons to be made, but Moore and Kajikuri,[6] using homografts in smaller dogs than ours, have obtained a 48 per cent patency figure in femoral artery replacement for periods of up to 182 days. Their grafts, however, were considerably shorter than those used here.

Incorporation of the prosthesis in the tissues was satisfactory; the inertness of nylon was demonstrated again. The rapid loss of strength found in these grafts (76 per cent in 30 weeks) confirms the findings of Harrison and Adler[4] who reported an 83 per cent loss after 6 months' insertion in the tissues but no further degeneration up to 495 days. In our limited studies there was no evidence that fatigue at the flexion site was a factor in this degeneration since they broke no more readily in this position than elsewhere, whether thrombosed or patent. Such degeneration was not prevented by siliconing the tube prior to

Fig. 8.

Fig. 7.

Fig. 7.—Transverse section. The nylon filaments of the graft have dissolved completely (bottom third), leaving only scanty cells and much amorphous material. The top part is the thick fibrocellular tissue which lines the tube and in the peripheral layers of which there are widely dilated capillaries. The crescent-shaped mass on the surface is post-mortem thrombus. (P.T.A.H. ×180.)

Fig. 8.—Transverse section. This specimen was occluded. The spaces were occupied by nylon filaments, which have been dissolved. Capillaries and collagen fibers pass through the pores in the wall of the prosthesis. (P.T.A.H. ×360.)

insertion. This is a serious indictment of the use of nylon in such prostheses. According to Edwards,[2] treatment with formic acid appears to modify the tendency of crimped nylon grafts to lose strength after implantation but it is as yet too early to arrive at a final assessment. Even if nylon does lose strength the apparent stabilization reported by Harrison and Adler[4] may leave a graft with a sufficient reserve to enable it to be used with safety. However, it is felt that, in regard to the Davenport prosthesis here described, manufacture with material other than nylon is desirable and a tighter weave is required, even if flexibility is reduced to some extent. This is being proceeded with.

SUMMARY

1. A new type of all-nylon arterial prosthesis is described with improved flexibility and noncollapsibility.

2. Experience in replacement of segments of the arterial tree in the dog is described.

3. Seventy-six per cent loss of strength of the warp was recorded after 30 weeks' implantation in the tissues.

4. Development is proceeding but has not reached the stage in which human use is justified as yet.

Histological Observations

METHODS

The grafts were fixed intact in neutral 10 per cent formalin, and numerous sections, both transverse and longitudinal, were subsequently taken from each specimen. These samples were obtained with only moderate difficulty, for nylon tubes which have been in the tissues for some time, as in the present study, are noticeably more friable and cut more easily than at the time of insertion. Most implants were covered by a layer of fibrous tissue, which in some cases was an exceedingly thin, delicate membrane. One graft was embedded in a large mass of vascular fibrous tissue and pus; another lay within a blood-filled cyst. After dehydration, the nylon was dissolved by placing the blocks of tissue in pure phenol for 18 hours at 56° C. This was followed by several hours in absolute alcohol at room temperature, prior to clearing in xylol and embedding in paraffin wax. Sections were cut 8 to 12 μ in thickness. Staining methods included Ehrlich's hematoxylin and eosin, the phosphotungstic acid hematoxylin (P.T.A.H.) and Weigert's methods for fibrin, van Gieson's solution for collagen, and Verhoeff's technique for demonstrating elastic tissue.

MICROSCOPIC APPEARANCES

A number of grafts are enclosed almost entirely within fat, with little or no fibrous tissue. Most of the implants, however, have a thick "adventitia" of collagen, with the fibers tending to run concentrically. This tissue fills the depressions between the nylon multifilaments (Figs. 7 and 9). Although this connective tissue sheath is not unduly vascular, large numbers of capillaries extend from it through the pores in the wall of the graft to the lumen (Fig. 8).

Amorphous, eosinophilic material and cells, often multinucleate, are found in and around the nylon multifilaments (Figs. 7 and 9). Occasionally, collagen fibers also ramify among the fine filaments.

Patent Prostheses.—All but one of these possess a thick "intima" which in some cases reduces the lumen of the nylon tube by half. The lining is densely collagenous, but many fibroblasts and capillaries are still present. These cells and fibers invariably lie parallel to the lumen (Figs. 7 and 9). The surface in contact with the blood stream undulates slightly but is always smooth and sharply defined, often by a refractile hyaline band of collagen, beneath which flattened nuclei are numerous (Fig. 10). Elastic tissue is not detected. Islands of unorganized fibrin are present among the fibers of the "intima" (Fig. 9), and a few fat cells may also be found; degenerative changes are not seen,

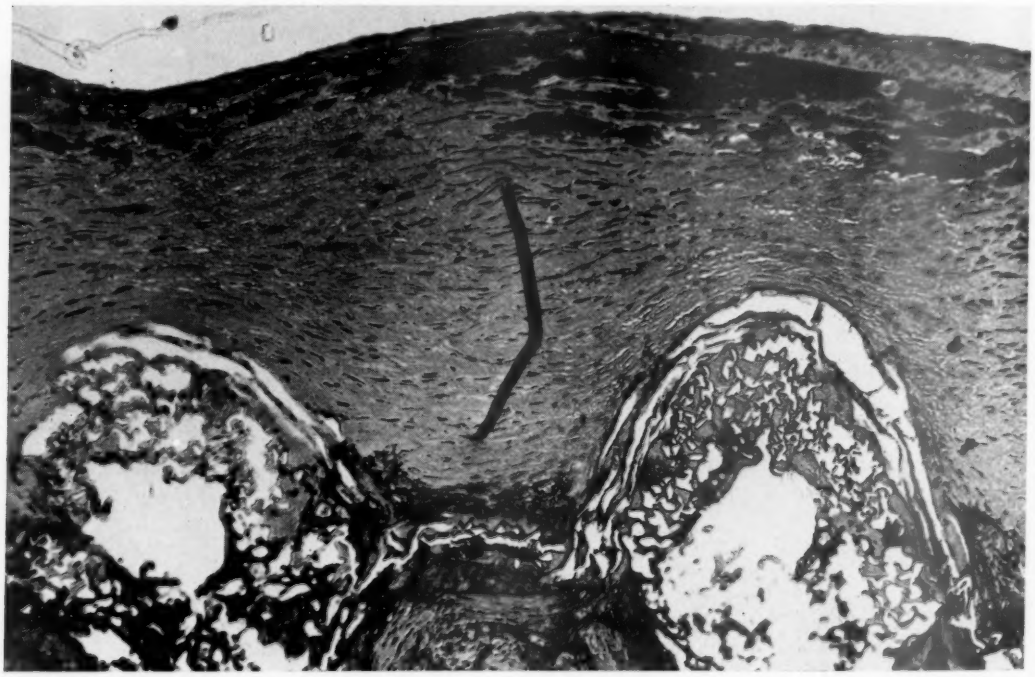

Fig. 9.—Longitudinal section. The fibrous tissue lining the graft undulates slightly. It fills in the gap between the nylon fibers, which have been removed. The dark-staining substance lying in the "intima" near the lumen is fibrin: this is an uncommon feature. (P.T.A.H. ×300.)

however. The connective tissue fills the hollows between the nylon fibers, and in this peripheral zone the capillaries are greatly dilated (Fig. 7). Only one graft is still lined by fibrin (Fig. 11). This implant is surrounded by blood clot, which has effectively insulated it from the tissues; capillaries and fibroblasts are thus unable to penetrate the porous implant in numbers sufficient to organize the fibrin lining the tube. However, endothelial cells cover the surface, apparently after migration from the arterial intima.

Occluded Prostheses.—Most of these are filled by soft, reddish, partly organized thrombus. There is abundant, somewhat myxoid, connective tissue, along with unorganized fibrin and blood clot. Hemosiderin-laden macrophages

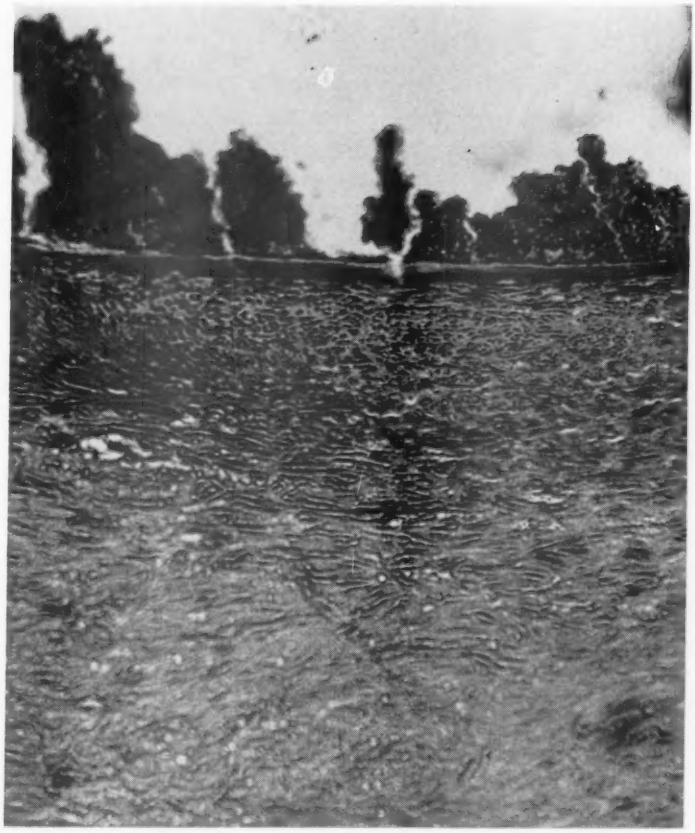

Fig. 10.—Transverse section. Irregular masses of post-mortem thrombus in the lumen rest on the smooth lining of the graft. The hyaline band which is in contact with the blood stream is clearly seen. (P.T.A.H. ×400.)

Fig. 11.—Longitudinal section. In this specimen the lining still consists of fibrin, in which a few cells float. A prominent endothelial lining is present. The debris which surrounds the nylon is seen at the bottom. (Hematoxylin and eosin ×1,500.)

are relatively few. Although the central area of most specimens consist of cystic spaces, full of watery fluid, in which small numbers of erythrocytes float, in some it is occupied by fairly dense connective tissue. In no instance, however, are the fibers and blood vessels arranged concentrically. In most, in fact, these structures run radially (Fig. 7) to and from the pores in the wall. This is seen particularly well in the 3 specimens in which the lumen is almost completely filled with fatty tissue. The "adventitia" of this group is also entirely fatty. As in the patent group the capillaries tend to be very large in the vicinity of the graft wall.

Arteries.—The vessels to which the prostheses are joined show minimal signs of damage to the tunica media. Loss of nuclear staining is confined to a few small foci at the anastomoses. When the graft is patent, the intima is usually normal, but, in a few, a rapidly tapering fibrous thickening is present. When the specimen is occluded, vascular fibrous tissue fills the lumen for a variable distance; this is denser and more homogeneous than that filling the graft itself. It usually extends as a greatly thickened intima for some distance along the artery, and the concave surface facing the blood stream is covered by a prominent endothelium.

DISCUSSION

That nylon, the material of which these prostheses are made, is only very slightly irritant to the tissues[1] is confirmed by the restricted cellular response to the nylon filaments and by the fact that several grafts lacked a definite capsule and were surrounded almost entirely by fat, with only occasional thin strands of collagen. The fairly substantial fibrous "adventitia" which most specimens acquire, therefore, results no doubt from organization of the thrombus which forms at the time of insertion, when blood oozes through the porous wall of the graft. Similarly, organization of the thrombus coating the internal surface produces the thick fibrocellular "intima" seen in nearly all patent specimens, and in fact, fibrin remnants sometimes persist among the collagen fibers (Fig. 9). This inner layer of thrombus is probably organized rapidly, in view of the large numbers of capillaries which penetrate the graft wall from the surrounding tissues. It is not clear why these vessels are often greatly dilated in the peripheral zone (Fig. 7). However, the structure of this lining of dense connective tissue is remarkably uniform with some increase in cellularity toward the lumen. Elastic tissue and smooth muscle, described by Hiertonn,[5] were not found; nor did degenerative changes, such as atheroma, occur in any patent graft or in the intima of the artery concerned. Although fibrin is seen at times within this layer, in no instance was ante-mortem thrombus found on the surface; this was invariably smooth and covered often by a dense hyaline band of collagen. There was no evidence, therefore, for supposing that the lumen inevitably narrows in time by incorporation and organization of successive layers of fibrin deposited on the surface. Certainly, distinct lamination is lacking in the tissues found in the lumen of occluded prostheses. Macroscopically, too, the material filling these closely resembled semiliquid, partly organized whole blood clot.

Patent implants did not have a distinct layer of cells which might be described as endothelial. Such a layer was seen clearly only in that specimen which was enclosed in blood clot and in which, therefore, the fibrin lining remained unorganized. Prominent endothelial cells, presumably from the adjoining arterial intima, covered the surface, however.

From these results it is clear that the porosity of a graft is of considerable importance. It leads to rapid replacement of the fibrin lining by cellular tissue, and consequently the graft is anchored within a double layer of fibrous tissue.

SUMMARY

1. Nylon prostheses of the type used here are firmly incorporated in connective tissue and when patent acquire a smooth lining of fibrocellular tissue.

2. Occluded specimens contain only partly organized whole blood clot, and there is no reason to believe that the lumen of patent specimens tends to narrow in time, from deposition and organization of fibrin.

We are very grateful to Professor R. P. Jepson who has given constant encouragement in this investigation. We should also like to thank Miss S. A. Winn, Mr. W. H. J. Coombs, M.S.R., Mr. F. D. Naylor, and many others who have assisted in the investigation; Messrs. Davenport Ltd. for their continual cooperation; the Staff of the University of Sheffield Animal House for their care of the dogs; Mr. A. S. Foster, Medical Artist, and the Photographic Department of the Sheffield Royal Infirmary for the illustrations.

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PATHOLOGIC AND RADIOGRAPHIC STUDIES OF AMPUTATED EXTREMITIES

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THERE has been a renewed interest in arteriosclerosis in the legs since the advent of arterial grafting. This paper presents a simple method of arteriography used for radiographic and pathologic study of 37 amputated legs in our Department of Surgical Pathology. An illustrative series of cases and illustrations demonstrates the value of these studies for the surgeon and the pathologist. The arteriograms furnish a map of the arteries of the amputated legs, have aided the pathologist in his dissection, and have directed his attention to occlusions, narrowing, and other findings of interest. Some of these legs were amputated after failure of artery grafts or endarterectomy. Other specimens were reamputations after failure of earlier amputations below the knee. Examinations of these specimens have revealed reasons for failure of these operations and have interested the various surgeons who submitted the specimens. Also the comparison with the preamputation arteriograms of the same extremity has aided in the roentgenologists' and clinicians' interpretation of the previous findings, in following the progression of the disease, and occasionally also in the etiologic diagnosis of thromboangiitis obliterans.

METHODS AND MATERIALS

The 37 legs had been amputated by various surgeons for gangrene or tumors. The indications are listed in Table I. Many methods for radiographic study of amputated extremities have been described and are helpful for certain special purposes. We have found that the simple method herein described, however, is adequate for most purposes. Fig. 1 shows the apparatus. Fig. 2 shows part of such an arteriogram of a leg amputated for fibrosarcoma. The vessels are normal. The entire arterial tree including the plantar arteries is clearly visualized.

TABLE I

Failure of conservative amputations	8
Failure of artery graft or endarterectomy	5
Thromboangiitis obliterans	3
Arteriosclerotic gangrene	16
Tumors, malignant neoplasms	5
	37

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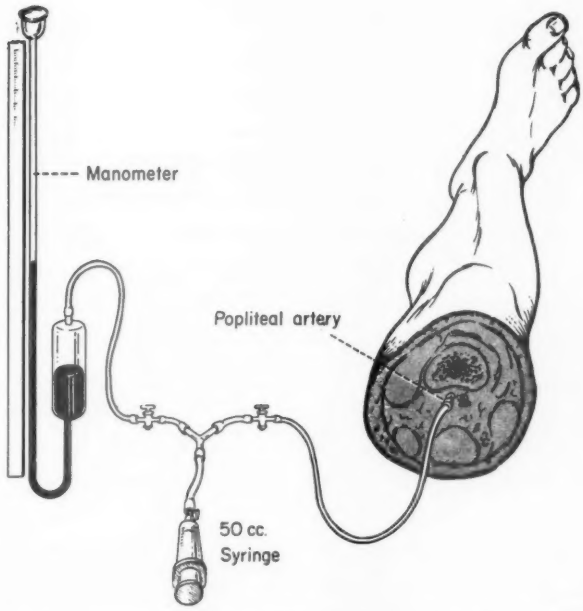


Fig. 1.—Apparatus for arteriogram of amputated legs.

Fig. 2.—Arteriogram of leg amputated above the knee for fibrosarcoma. Films of the foot demonstrate the detail obtainable in such arteriograms.

The technique is as follows. Polyethylene tubing of appropriate size, usually 4 mm. in diameter, is secured in the popliteal vessel with large silk ligatures. Repeated transection distally may be necessary to find a segment partially open. The artery is frequently occluded or markedly narrowed at the level of transection. However, a satisfactory map of the arteries of the leg can almost always be obtained in spite of marked narrowing or occlusion of segments. For legs amputated below the knee the posterior and anterior tibial and the peroneal arteries are separately cannulated and the tubing is connected so that they are simultaneously injected. Obviously the tubing must be filled without bubbles.

Scout films of the specimen are taken prior to the injection in order to check the position of the extremity, to check the radiographic technique, and to observe calcification of the vessels.

The apparatus as illustrated in Fig. 1 shows the manometer used to control the pressure. Also it should be noted that sufficient tubing is used so that the hands of the pathologist are not in the x-ray beam. The radiologist follows precautions, such as shields, aprons, and the use of cones to prevent scatter, for the safety of the personnel. These are essential.

It is necessary to avoid opacification of the veins by limiting the volume of dye in the first injection. Furthermore, unless one avoids repetition of the injection, the soft tissues will become opacified. These difficulties can be avoided and satisfactory films obtained with one injection, by good teamwork with the radiologist, correct volumes of dye, and injection under controlled pressure with the simple apparatus as diagrammed.

Table II shows the volume of dye for the initial injection. The dye used is 30 per cent sodium diprotrizoate, Miokon.* This is a low-viscosity water-soluble medium which gives good opacification of the arteries. There is no residue in the microscopic sections.

TABLE II. VOLUME OF DYE FOR VARIOUS SPECIMENS

SPECIMEN	VOLUME 30% MIOKON
Hemipelvectomy	40-50 c.c.
Hip disarticulation	35-45 c.c.
Mid-thigh	30-40 c.c.
Low thigh	20-30 c.c.
Below the knee	15-25 c.c.

The first film is usually an anteroposterior one with the leg in 20 to 30 degree internal rotation. In this position the distal popliteal and upper outflow tract is not obscured by overlying bone.

Injection is made at a rate which holds the pressure at 60 mm. Hg during the injection. The film is exposed immediately on signal of the pathologist, then the leg is turned for a lateral view, and 5 to 10 c.c. more dye is injected. If films of the foot are desired, the specimen is moved and another 5 to 10 c.c. of dye is injected. With the surgical pathologist injecting and positioning the specimen and the radiologist exposing and changing film casettes, the arteriograms may be completed in 5 minutes. Stereoscopic views are helpful but not necessary.

*We are grateful to the Mallinckrodt Chemical Works for their generous supply of Miokon.

After inspection of the arteriogram the pathologist dissects the specimen with particular attention to those areas of most interest. Blocks are taken 1 cm. thick including artery, vein, and nerve at various levels. These are fixed in formalin for 24 hours and then trimmed to the usual size and thickness for clearing, embedding, and sectioning.

Dissection of peripheral arteries is time-consuming work and this is facilitated when they are injected before dissection. Pathologic changes can be localized without opening the artery. Furthermore, it is frequently difficult by dissection alone accurately to evaluate the *degree* of patency. The arteriogram supplies a map of the arterial tree for later reference and comparison with the dissection and microscopic slides. Arteriograms after amputation visualize the collateral circulation in small arteries which is visualized in more detail than in the preoperative arteriograms.

Various modifications and improvements have been reported for the study of amputated extremities and cadavers. These include the addition of gelatin in order to form a cast of the lumen.[4, 5] Others have injected media of various colors into different arteries in order to trace the distribution of material by dissection. Some have removed the bones and unrolled the soft tissues so that all the vessels are in one plane.[5] The present method is simpler than any of these, but, of course, for special purposes various modifications of these older methods can be used.

ARTERIOSCLEROSIS

The following cases illustrate the value of this clinicopathologic correlation.

Case 1. Early Thrombosis of Femoral Artery Homograft Due to Distal Stenosis of the Popliteal Artery.—Mrs. B., a 58-year-old woman, was admitted with incipient gangrene of a painful right great toe; there were no pulses below the common femoral artery. Bilateral femoral arteriograms showed a short block of the superficial femoral artery with marked proximal and distal intimal thickening. The great toe was amputated but pain continued and discoloration progressed proximally. Four days later a femoral artery homograft was inserted to bypass the femoral block. The graft clotted and reoperation was necessary the following day. Eight days after the graft, an AK amputation* was performed.

Pathologic examination (SP #55-3788): The graft and proximal popliteal artery were filled with fresh thrombus. The homograft was thrombosed due to marked segmental narrowing of the popliteal artery 2 cm. distal to the site where the graft was implanted (Fig. 3). Cannulation and injection of the distal popliteal artery showed fair outflow.

Comment: This is the most common cause of early thrombosis of artery grafts. This and similar cases served to emphasize the need for more adequate exposure of the popliteal artery and insertion of grafts distal to areas of stenosis. In this and in several other cases, the distal popliteal artery was open when the proximal was obstructed (Fig. 4).

Careful autopsy study of 356 limbs by arteriograms and dissection has shown conclusively that the popliteal artery is most likely to be normal distal to the knee joint.[4]

Case 2. Failure of Transmetatarsal and Below the Knee Amputations Due to Progressive Thrombosis.—This 60-year-old man with diabetes (SL 10003 VAH) had wet gangrene of several toes. There was no rest pain, but some signs of diabetic neuropathy. He had strong popliteal pulses. Preamputation arteriogram showed widespread intimal plaques and narrowing. The transmetatarsal amputation was left open in order to drain the plantar sepsis. The

*Abbreviations used in this paper include "AK" and "BK" amputation for amputation above and below the knee, respectively.

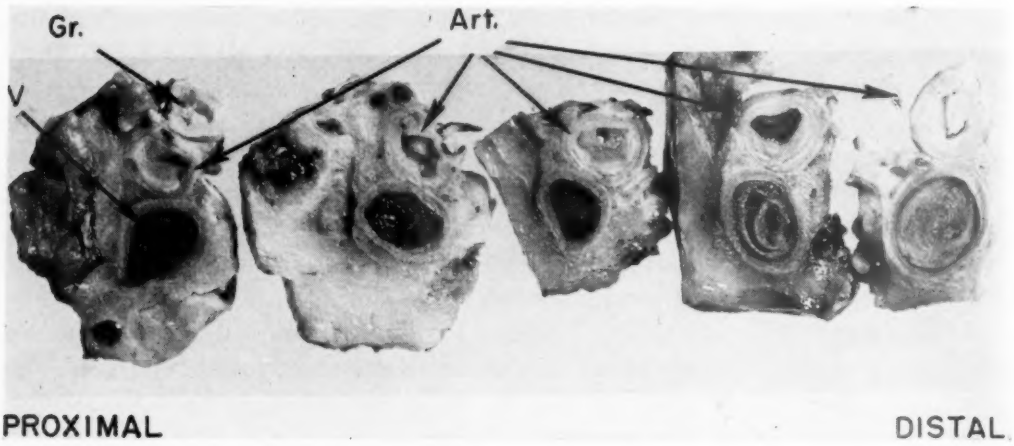


Fig. 3.—Case 1. Early failure of bypass femoral artery homograft. Cross sections show stenosis of the popliteal artery (*Art*) distal to the graft (*Gr*) and proximal to the knee joint. Distal to the knee joint the outflow is good. The popliteal vein (*V*) is thrombosed.

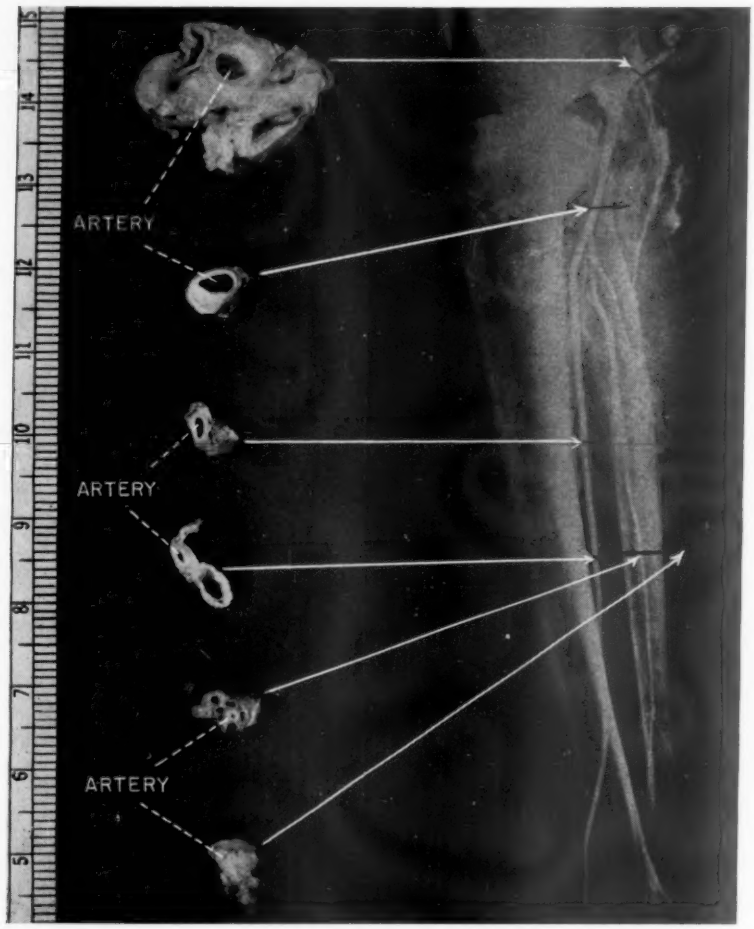


Fig. 4.—Leg amputated for gangrene. Upper popliteal artery (not shown on the film) was completely occluded. Distal popliteal artery seen on film and cross section is open. Arrows show the sites of the cross sections.

wound granulated and was healing nicely. Two months later, however, sepsis recurred beneath the healing plantar flap. The posterior tibial pulse had disappeared. Plantar sepsis progressed despite further drainage and 3 months later amputation below the knee was performed. The surgeon reported satisfactory bleeding at the amputation site.

Postamputation arteriogram (BK specimen S2336-56) (Fig. 5): The extensive intimal disease noted in the preoperative arteriogram was confirmed. The specimen revealed that the failure of the transmetatarsal amputation was due to recent thrombosis of the distal one-third of the posterior tibial artery and an old occlusion of the distal anterior tibial artery.

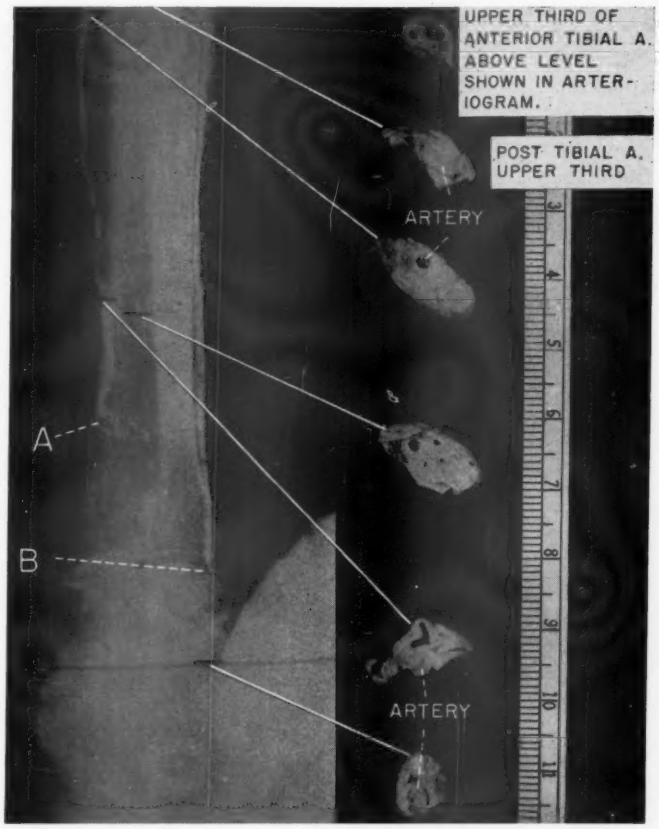


Fig. 5.—Case 2. Arteriogram of leg amputated below the knee after failure of transmetatarsal amputation. *A* shows old occlusion of posterior tibial artery. *B* indicates site of recent thrombosis of anterior tibial artery.

Postoperative course: After an apparently satisfactory convalescence, the anterior flap of the BK amputation showed necrosis at the central edge of the suture line. This progressed and finally amputation was performed above the knee.

Postamputation arteriogram (AK specimen S 56-2510) (Fig. 6): A stenosis of the anterior tibial artery at the hiatus in the interosseus membrane was noted, but the artery was open for a considerable distance. This stenosis is not revealed in the routine anteroposterior films. Lateral films showed that the lumen was markedly narrowed at that site.

Comment: Arteriograms are done on our surgical service prior to any amputation in order to select patients for possible arterial grafting. The value of arteriograms in selecting levels of amputation is still under investigation.

Radiographic Features of Arteriosclerosis.—Most amputated extremities show advanced changes of arteriosclerosis, such as occlusions, thickening of the wall, or calcification. These findings have been well described in patients with

symptoms of arterial insufficiency. The findings in earlier stages when arteriosclerosis of the legs may be asymptomatic also have been described in detail.[4] Arteriograms of amputated extremities, however, show more detail and can be checked by the gross dissection and microscopic appearance. No aneurysms were present in the legs studied.

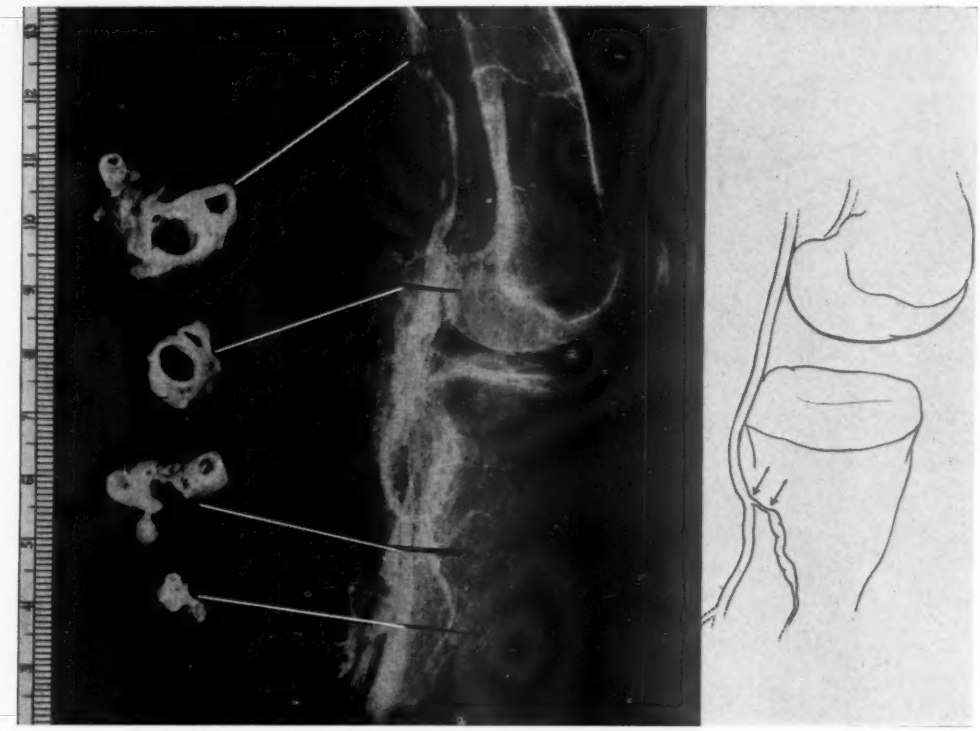


Fig. 6.—Case 2. Arteriogram of leg amputated above the knee after failure of BK amputation. Radiolucent filling defect in upper popliteal artery is postmortem clot. There is marked narrowing of the anterior tibial artery at its hiatus in the fascia. This zone is shown in the sketch of the arteriogram.

Occlusion.—Threadlike postmortem clots are often found in pathologic arteries. They are not obstructing and the nonviscous Miokon flows readily around them. They are distinguished readily from antemortem clots. The arteriograms rarely show unfilled but nonoccluded segments between occlusions. The thin media readily enters via collaterals, although occasionally a small second injection, in order to get a lateral film, fills such narrowed segments. In one leg the anterior tibial artery was hypoplastic and did not extend to the foot. In this leg the dorsalis pedis was an extension of the peroneal artery. Absence of an artery or an anomalous course of the artery is easily differentiated from an occlusion because in the latter collateral vessels are obvious. Furthermore the dissection reveals the aplasia or absence. In amputated extremities the occlusions are so widespread that no typical pattern is apparent. In the popliteal artery the occlusions are most frequently proximal to the knee joint. Air which may be inadvertently injected makes small round radiolucent filling defects and causes no misinterpretation.

Partial occlusion due to localized intimal plaques is most common at sites of branching. Intimal thickening is seldom concentric in arteriosclerosis. The intima is almost always irregular when thickened. These plaques are widespread usually throughout the length of the unoccluded parts of arteries. Intimal thickening on the front or back walls causes no change in width of the column and may be detected only because of slight changes in the density of the dye column. Plaques on the sides of the arteries are readily visible as changes in the width of the dye column. Calcification of medial or intimal types or both was frequently seen on scout films.

Precautions.—In almost every instance, the occlusive disease and intimal thickness are more severe than they were estimated to be from the arteriogram. Lateral films were helpful, however, and occasionally revealed narrowing which was not apparent in the conventional anteroposterior view. Variations in density of the dye column are just as significant as narrowing but are not revealed when concentrated dye is used. Blunting of a bifurcation is another early change occasionally observed.

Pathologic Findings in Arteriosclerosis.—Pathologic alterations of arteriosclerosis in the legs examined showed every possible change. The changes were most advanced at areas of bifurcation (Fig. 7). The upper popliteal artery was more frequently narrowed or occluded than the distal artery. Anterior and posterior tibial and peroneal arteries showed no characteristic localizations. Changes in the small arteries of the foot were less advanced. Occlusions were frequently segmental. There would be almost complete obstruction then a fairly normal lumen and then again almost complete obstruction. Recent thrombi would sometimes cause sudden occlusion particularly at points of branching (Fig. 8). With the formation of thrombi, calcification, and plaques, there was often irregular destruction of the wall (Fig. 9) so that at times the media was eccentrically involved. In some areas the wall of the vessel was made up of plaques, thrombi, with no evidence of media, and only adventitia. Bone formation is commonly seen in advanced arteriosclerosis of the lower legs (Fig. 10). This bone formation may be so extensive that bone marrow may be present. The eccentric destruction of the wall of vessels in the presence of calcification or bone makes endarterectomy difficult. Changes in artery grafts after varying periods of implantation have been reported by others. One of the first grafts recovered from an amputated extremity and samples of this same graft submitted at the time of operation showed striking ice crystal artefacts (Fig. 11). The artery bank techniques were improved and artery grafts were frozen more rapidly. Thereafter ice crystal artefacts were rarely seen.[2]

THROMBOANGIITIS OBLITERANS

With the advent of arteriography, more thorough study of this disease is possible. Clinicopathologic correlation is aided by arteriograms of such patients and their amputated extremities.

Fig. 7.—Arteriosclerosis. Eccentric prominent intimal thickening with recent occlusions of anterior and posterior tibial artery near their origin. (×5, ⅕ off reduction.) (WU Neg. 58-831.)

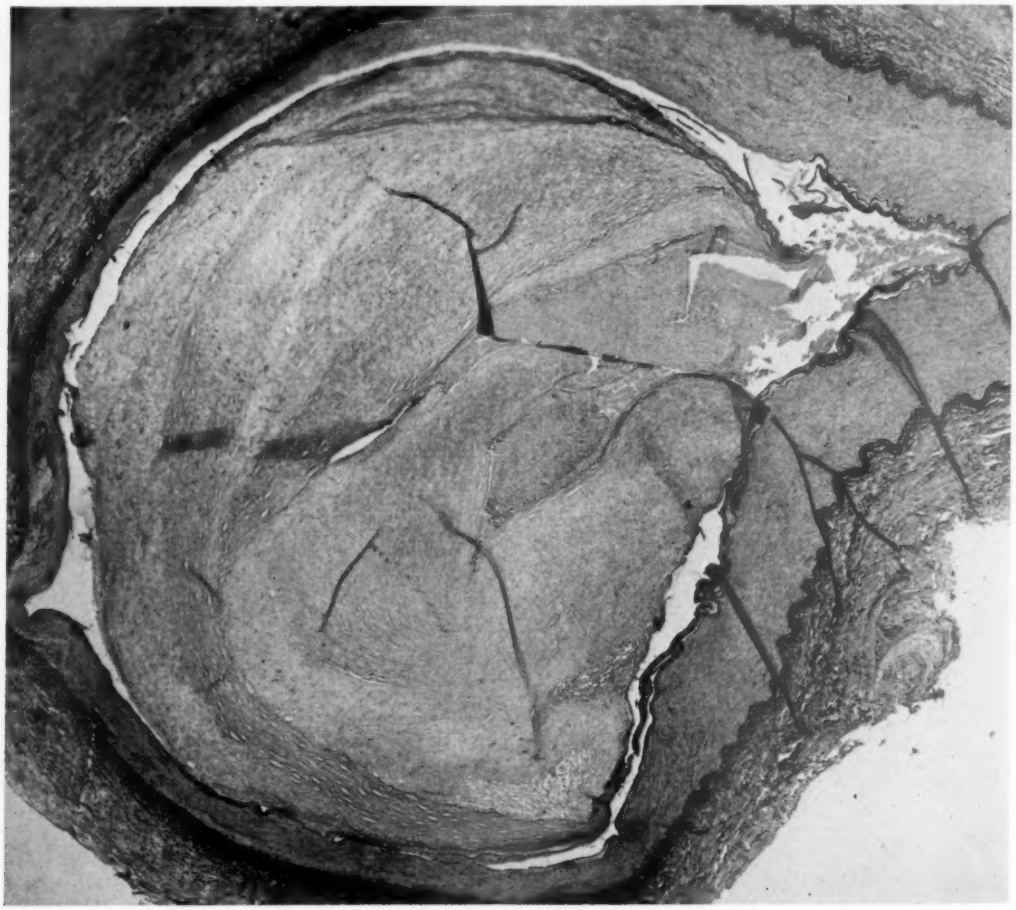


Fig. 8.—Arteriosclerosis. Recent complete thrombosis near bifurcation of popliteal artery. (Low power.) (WU Neg. No. 58-833.)

Case 3. Thromboangiitis Obliterans (Active).—This 23-year-old white man (SL 5543 VAH) was admitted for pain and discoloration of the left great toe. He had had intermittent claudication of the calves of his legs since the age of 21 and had a similar episode at that time.

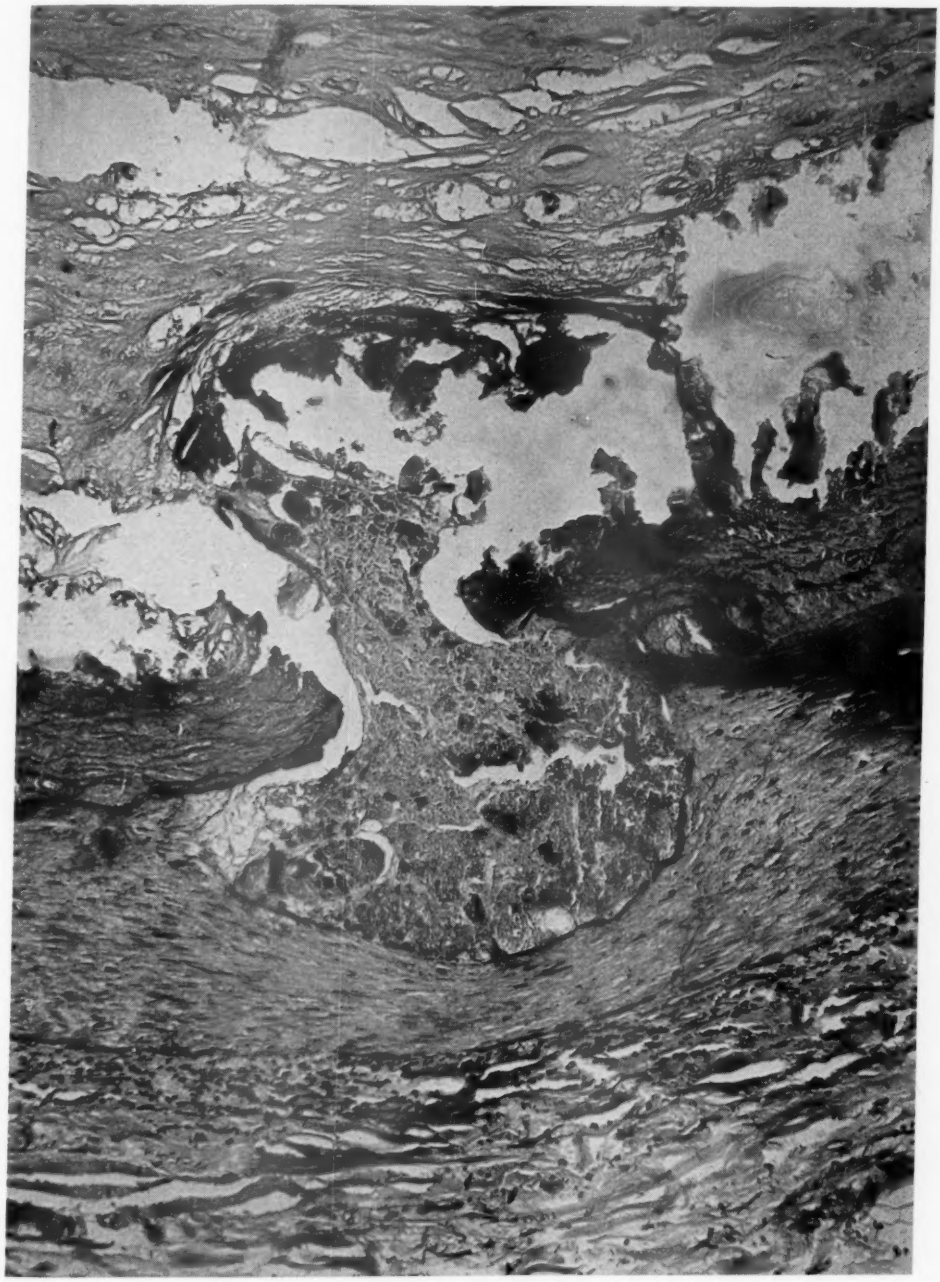
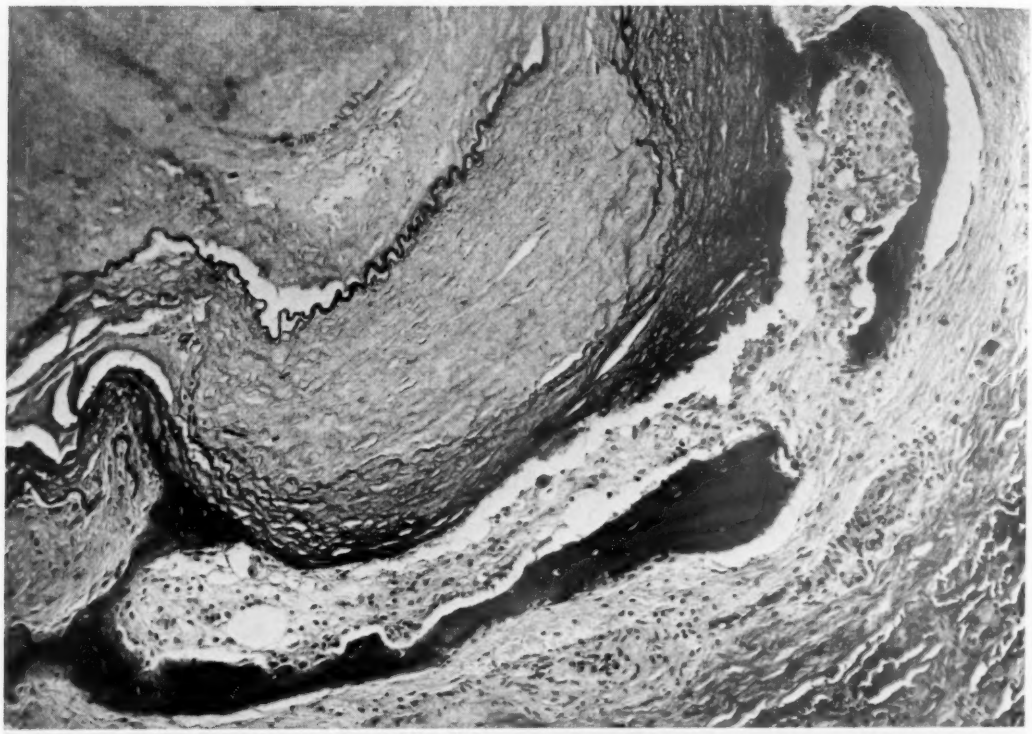


Fig. 9.—Arteriosclerosis. Erosion of intimal plaque with hemorrhage and rupture of media of the artery. (Low power.) (WU Neg. 58-829.)

Past history: He had an ischemic ulcer of one finger tip several years ago. He continued to smoke several packages of cigarettes daily and had recurrent attacks in spite of lumbar and cervical sympathectomies. Physical examination at the present admission showed

Fig. 10.



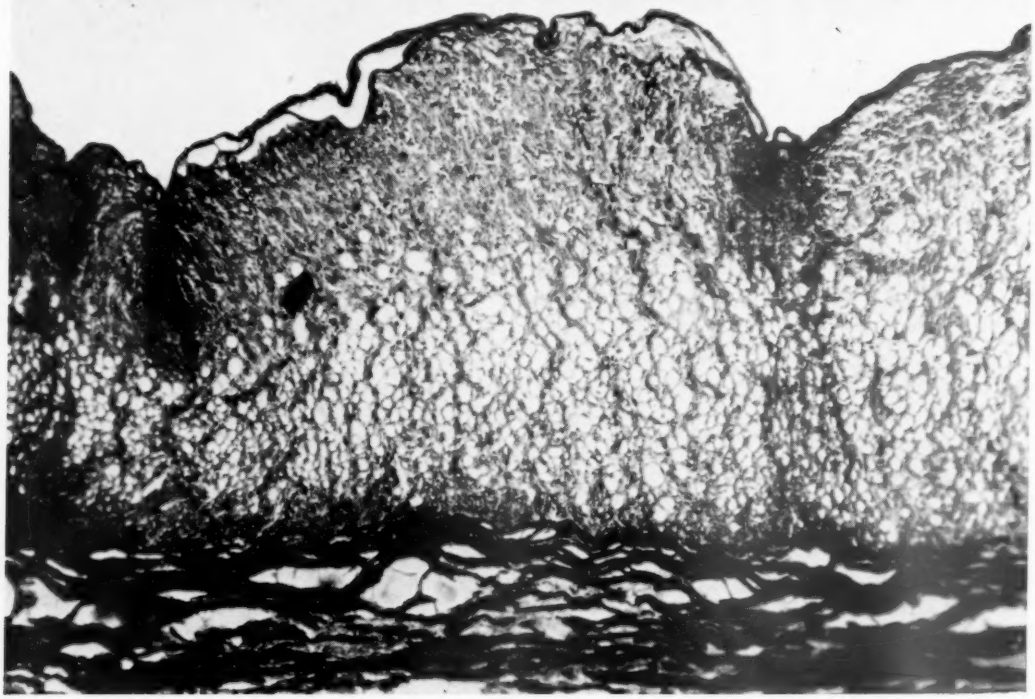


Fig. 11.

Fig. 10.—Arteriosclerosis. Prominent bone formation in wall of artery. (×130, ⅓ off reduction.) (WU Neg. 58-642A.)

Fig. 11.—Freeze-dried artery homograft. Striking ice crystal artefacts in wall of artery. (×150, ⅓ off reduction.) (WU Neg. 58-638A.)

absent pedal pulses, cyanosis of the toe, and a chronic paronychia of the great toe. Arteriogram (Fig. 12) showed normal femoral and popliteal arteries and no calcification, intimal irregularity, or plaques. The anterior tibial artery tapered and was occluded in the lower one-third of the leg. Below this occlusion it refilled via collateral from the posterior tibial artery for a short segment but was occluded again on the dorsum of the foot and recanalized

Fig. 12.—Case 3. Thromboangiitis obliterans. Arteriogram prior to amputation. *A* and *B* indicate ends of an open segment of peroneal artery serving as collateral for the foot. However, it is occluded proximally and narrowed distally. *C* indicates recanalized segment of occluded posterior tibial artery.

with tortuous threadlike lumen. The upper peroneal artery was not visualized. The posterior tibial artery tapered and became occluded and recanalized just above the level of the medial malleolus (Fig. 12, *B*). After failure of a prolonged trial of conservative therapy, the leg was amputated below the knee.

Pathologic examination (S 2191-55): The postamputation arteriogram confirmed the findings described and served as a guide for the dissection. As is customary, some small vessels and collateral were seen which were not visible in the arteriogram prior to amputation. The microscopic sections showed a few areas where inflammatory cells were present in the media of one occluded artery. The veins, nerves, and artery in all occluded segments were surrounded by dense scar tissues. In some occluded areas there was thrombosis and recanalization of the arteries and veins. The larger arteries were entirely normal.

Discussion: The diagnosis of Buerger's disease was made because of the clinical and pathologic picture. The salient features were (1) arterial insufficiency of all 4 extremities and (2) the arteriographic appearance which showed no evidence of intimal plaques or calcification. There were smooth tapered occlusions with threadlike recanalization. Little collateral circulation was seen in pre- and postamputation arteriograms, (3) neither arteriography nor careful pathologic examination of the BK specimen revealed intimal plaques or calcification, and (4) the microscopic findings were consistent with the diagnosis of Buerger's disease.

Fig. 13.—Case 4. Thromboangiitis obliterans. Arteriogram of leg amputated above the knee. *A* indicates tapered end and recanalized peroneal artery. *B* shows site of occlusion of posterior tibial artery.

Case 4. Thromboangiitis Obliterans (Chronic).—A 47-year-old white man was admitted for painful blue great toe of several weeks' duration. For the past 16 years (that is, since the age of 31) he has had 4 hospital admissions for the same complaint. Six years ago he had a partial but persistent hemiplegia. Carotid angiograms at that time showed a diffuse narrowing of the internal carotid artery for several centimeters in its mid-portion. Biopsy of the

Fig. 14.

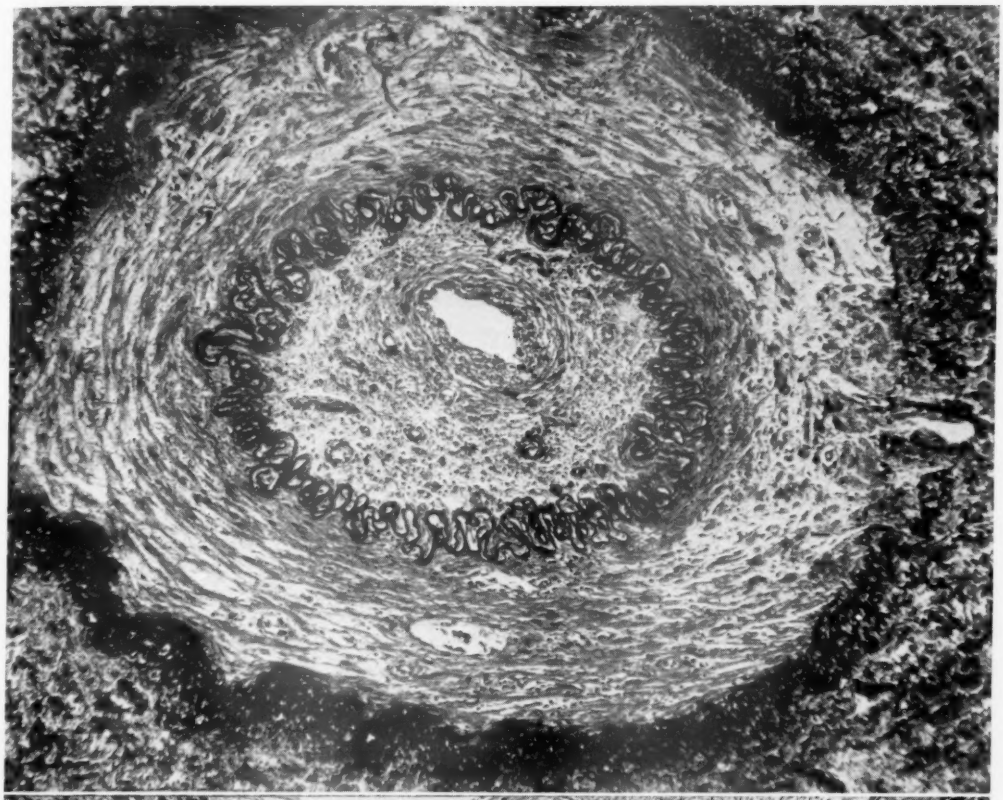


Fig. 15.

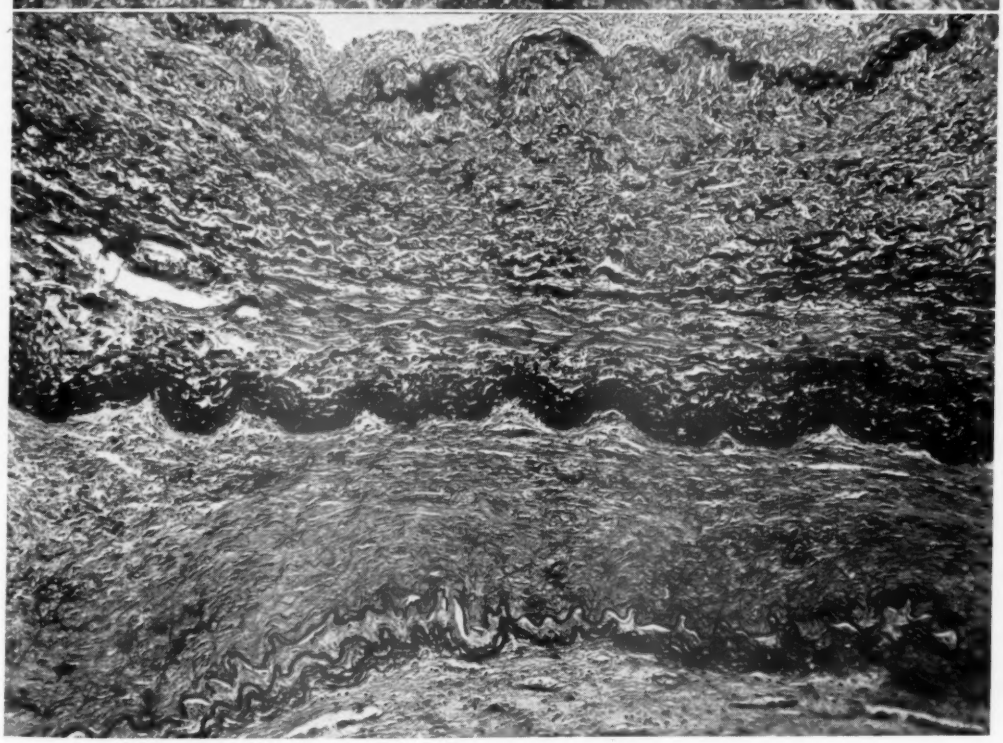


Fig. 14.—Case 4. Thromboangiitis obliterans. Cross section of peroneal artery shows old occlusion and recanalization. There is no cholesterol, no intimal plaques, or calcification. (×117, ⅙ off reduction.) (WU Neg. 58-810A.)

Fig. 15.—Thromboangiitis obliterans. Fusion of adjacent artery and vein by fibrous tissue which also enveloped the adjacent nerve. (×120, ⅙ off reduction.) (WU Neg. 58-808.)

right superior thyroid artery was taken during the carotid angiogram and showed no abnormalities. During this present admission the pain and discoloration of the toe and forefoot continued and required frequent narcotics. An amputation was performed above the knee.

Postamputation arteriogram (SP 55-1060 BK) (Fig. 13): There was no calcification, intimal irregularity, or other evidence of arteriosclerosis. The popliteal artery and all three of its main branches were open in the upper one-third of the leg. The posterior tibial artery ended at that level in a smooth tapered end. Distally the artery was almost entirely occluded, but there were segments in which recanalization had occurred, and the dye column was a narrow tortuous thread. The anterior tibial artery and the peroneal artery ended in midcalf. There were very few small arteries, and little collateral circulation was visible.

Pathology: The microscopic sections were consistent with thromboangiitis obliterans in the chronic phase. There was extensive fibrosis surrounding nerves, arteries, and veins with old thrombosis and recanalization of both the veins and the arteries. No calcification and no intimal plaques, fat, or cholesterol were found (Fig. 14).

Discussion of Thromboangiitis Obliterans.—Thromboangiitis obliterans (Buerger's disease) has been well described in the literature. The classic pathologic findings however are seldom found. Furthermore, arteriography and careful dissection of the vessels and careful pathologic examination of amputated limbs reveals that the commonest cause of arterial insufficiency in young men is ordinary arteriosclerosis. Buerger's disease is so rare that we have not found pathologic confirmation of a single instance of Buerger's disease at the Jewish Hospital of St. Louis (Hassan, personal communication, 1958). We have pathologic confirmation for three examples of what might be called Buerger's disease. In these cases there was no calcification of vessels seen radiographically or pathologically. There was evidence of segmental thromboses of arteries with recanalization of lumina (Fig. 14). There was also fusion between arteries and veins and at times fibrous tissue envelopment of nearby nerves (Fig. 15). Thrombosis of veins in these particular cases was of minimal importance. The pathogenesis of these lesions is obscure but it has been pointed out by Kelly[3] that similar changes might be produced by embolization, thrombosis, and recanalization. Gore[1] believes that the basic lesion is arterial thrombosis starting distally in small arteries. There was no evidence of any primary arterial inflammation in his cases.

It is clear that early and more frequent biopsies and arteriograms in early cases will be necessary to reveal the course of the disease and to clarify the diagnosis. However, the understanding of such patients is not improved by new names or by unifying concepts with the use of terms such as "obliterative arterial disease."

CONCLUSIONS

1. A simple method of arteriography of amputated extremities is described.

2. The arteriogram is a detailed map of the arteries which is a guide to the pathologist in his dissection and pathologic evaluation of the vascular lesions in an extremity.

3. Arteriograms and dissections of the amputated extremities are useful for the comparison and correlation with the preoperative arteriograms and have helped in more precise evaluation of these preoperative films.

4. A series of case reports illustrates the value of radiographic and pathologic study of amputated legs in the investigation of failures of conservative amputations, thromboses of arterial homografts, and other surgical complications.

5. Thromboangiitis obliterans is a rare disease characterized by noncalcific segmental occlusions. It has distinctive clinicopathologic and arteriographic findings. Its pathogenesis is obscure.

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THE LATE DEVELOPMENT OF GASTRIC CANCER AFTER GASTROENTEROSTOMY AND GASTRECTOMY FOR PEPTIC ULCER AND BENIGN PYLORIC STENOSIS

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GASTROENTEROSTOMY for benign pyloric stenosis or for peptic ulcers in the duodenum or stomach has been employed with considerable frequency and for such a long period of years that many of the younger subjects have lived long enough to allow for the possible evolution of gastric cancer. This relatively rare sequel of the conservative operation is being reported in increasing numbers, which fact stimulates the question as to whether or not the presence of a new stoma associated with simple gastroenterostomy or partial gastrectomy exerts any etiologic influence on the subsequent development of cancer within the stomach.

Incidence.—In the Memorial Cancer Center a survey of 1,623 case records of gastric cancer reveals that only 10 (1.1 per cent) of these patients had experienced previous gastroenterostomies or subtotal gastrectomies for ulcer. In a similar report from the Mt. Sinai Hospital of 1,160 patients with gastric cancer, only 0.4 per cent had undergone previous surgical treatment for benign conditions. In this regard, it is generally admitted that the coexistence of gastric cancer and duodenal ulcer is rare, even less frequent than one might expect for the incidence of the development of gastric cancer in the general population. In a report by Gray and Lofgren[17] from the Mayo Clinic and based upon an experience of 34 years, the conclusion was expressed that the association of duodenal ulcer and benign gastric ulcer was 12 times as frequent as the coexistence of duodenal ulcer and gastric cancer. They reported on 825 consecutive operations performed at the Mayo Clinic for stomal defects such as stenosis, marginal ulcers, malfunctioning anastomoses after previously constructed gastroenterostomies and in which the secondary operations performed by them consisted of subtotal gastrectomies; in this group of 825 consecutive gastrectomies performed at variable periods sequential to gastroenterostomies they encountered only 11 cases of gastric cancer.

Helsingen and Hillestad[18] of Oslo, Norway, in their attempt to solve the enigma of this relationship excluded all of their patients who had been operated upon less than 5 years before the development of gastric cancer in order to rule out the possibility that the neoplasm might have been present and undetected at the time of the original gastroenterostomy. In their patients with gastric ulcer the frequency of the later development of gastric cancer was 3 times as

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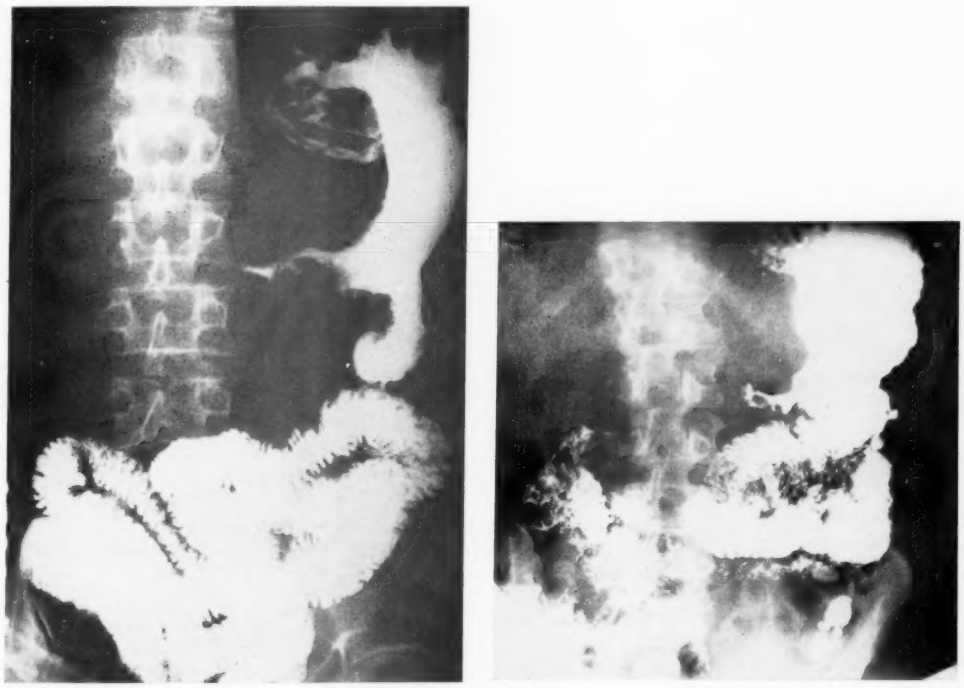
high as the expected or anticipated incidence in comparison with the general population of the same age group. In the case of their patients who had undergone these operations for duodenal ulcer, the observed and the expected frequencies of the subsequent development of gastric cancer were identical.

Time Sequence (interval between previous operation and the known onset of gastric cancer).—No one has knowledge of the approximate length of time required for the genesis of human gastric cancer, even when evolving from carcinoma in situ. In our 19 patients an average of 13 years elapsed between the performance of the gastroenterostomy or partial gastrectomy for benign ulcers or pyloric stenosis and the subsequent known onset of gastric cancer. The longest time that elapsed was 39 years in a patient who was 20 years of age at the time of gastroenterostomy. One of the 19 patients underwent gastroenterostomy at the early age of 20 years. One young woman at the age of 16 years was a patient. The average age in which our patients underwent the original operation of gastroenterostomy or gastrectomy was 41 years.



A. *B.*

Fig. 1.—*A*, Extensive carcinoma involving distal gastric segment, gastroenterostomy stoma, and lesser curvature. *B*, Late development of gastric cancer after gastroenterostomy for peptic ulcer. The neoplasm involves the margin of the stoma and the distal gastric segment.

Indications for Original Operation.—Sixteen of the 19 patients had duodenal ulcers (84 per cent); 2 patients had benign gastric ulcer (10.5 per cent); one patient had a subtotal gastrectomy for a reticulum-cell sarcoma in the distal segment of the stomach. This patient subsequently developed gastric cancer in the stomach remnant. Fifteen of the 19 patients had simple gastroenterostomies and 4 patients had subtotal gastrectomies of the conventional type.

TABLE I. THE LATE DEVELOPMENT OF GASTRIC CANCER FOLLOWING GASTROENTEROSTOMY

NUMBER CASE	SEX	PRIMARY OPERATION				DIAGNOSIS OF GASTRIC CANCER			
		AGE	YEAR	TYPE OF OPERATION	DIAGNOSIS	AGE	YEAR	INTERVAL (YEARS)	TREATMENT
1. R. P.	F	38	1918	Gastroenterostomy	Gastric ulcer	51	1931	13	Exploratory laparotomy
2. H. E.	M	61	1927	Posterior gastroenterostomy	Duodenal ulcer	65	1931	4	Exploratory laparotomy and x-ray therapy
3. A. R.	F	43	1929	Gastroenterostomy	Duodenal ulcer	45	1931	2	Exploratory laparotomy
4. A. C.	M	36	1929	Gastroenterostomy	Gastric ulcer	44	1937	8	Exploratory laparotomy
5. H. B.	M	52	1933	Posterior gastroenterostomy	Duodenal ulcer	61	1942	9	Exploratory laparotomy and x-ray therapy
6. P. W.	M	42	1939	Posterior gastroenterostomy	Duodenal ulcer	46	1943	4	Exploratory laparotomy
7. M. B.	F	45	1922	Gastroenterostomy	Duodenal ulcer	72	1949	27	Radical subtotal gastrectomy
8. F. K.	F	27	1942	Subtotal gastrectomy and x-ray therapy, 1,800 r., and 4 Gm. radium pack	Reticulum-cell sarcoma	34	1949	7	Radical total gastrectomy
9. A. R.	F	47	1948	Subtotal gastrectomy	Duodenal ulcer	50	1951	3	Radical total gastrectomy and distal esophagectomy
10. A. W.	F	32	1929	Gastroenterostomy	Duodenal ulcer	52	1949	20	Exploratory laparotomy
11. J. K.	M	60	1950	Posterior gastroenterostomy	Duodenal ulcer	62	1952	2	Radical subtotal gastrectomy
12. R. G.	M	52	1937	Posterior gastroenterostomy	Duodenal ulcer	67	1952	15	Radical subtotal gastrectomy
13. E. M.	F	16	1925	Posterior gastroenterostomy	Duodenal ulcer	43	1952	27	Exploratory laparotomy and biopsy
14. H. B.	M	29	1946	Gastroenterostomy	Duodenal ulcer	35	1952	6	Transthoracic vagotomy for diagnosis of marginal ulcer, 1 year later palliative jejunojejunostomy
15. L. F.	M	34	1927	Posterior gastroenterostomy	Duodenal ulcer	61	1954	27	Radical total gastrectomy
16. M. H.	F	20	1915	Gastroenterostomy	Gastric ulcers	59	1954	39	Exploratory laparotomy
17. F. G.	M	47	1932	Posterior gastroenterostomy	Duodenal ulcer	71	1956	24	Radical subtotal gastrectomy
18. W. S.	M	48	1949	Subtotal gastrectomy	Duodenal ulcer	56	1957	8	Exploratory laparotomy and x-ray therapy
19. B. S.	M	47	1947	Gastroenterostomy	Duodenal ulcer	57	1957	10	Exploratory laparotomy and x-ray therapy

OR SUBTOTAL GASTRECTOMY FOR PEPTIC ULCER OR PYLORIC STENOSIS

LOCATION OF CANCER	GROSS AND MICROSCOPIC DESCRIPTION	END RESULTS
Greater curvature	Small infiltrating adenocarcinoma, metastatic to ovaries	Died 7 months
Cardia and lesser curvature	Large infiltrating tubular adenocarcinoma	Died 6 months
Stoma and distal half of stomach	Large infiltrating adenocarcinoma	Died 3 months
Fundus of stomach	Adenocarcinoma	Died 16 months
Stoma and pylorus	Diffuse gelatinous adenocarcinoma	Died 9 months
Stoma	Extensive polypoid adenocarcinoma	Died 9 months
Stoma	Five polypoid tumors with adenocarcinoma at the base of two; there was also evidence of intestinal metaplasia about the stoma	Without evidence of cancer 8 years
Stoma	Three separate areas of gelatinous, signet-ring adenocarcinoma, negative nodes; no other organs show evidence of x-ray changes	Died 1 year
Stoma	Polypoid tumor involving remaining stomach and distal esophagus; mucosa shows no evidence of intestinal metaplasia	Died 4 months
Stoma	No sight of primary hypertrophic fold of mucosa with submucosal adenocarcinoma about the intestinal metaplasia is present	Died 3 months
Stoma	Polypoid tumor on proximal side of stoma; at the stoma there was typical epidermoid carcinoma and adenocarcinoma; metastases to perigastric nodes of adenocarcinoma only	Operative death
Stoma	A 6 by 5 cm. adenocarcinoma extending through serosa; there was mucosal thickening and attenuation about the tumor and microscopic squamous metaplasia in the tumor about the stoma	Without evidence of cancer 2 years, lost to follow-up
Unknown	No definite sight of primary seen at autopsy, only hypertrophied rugae with submucosal adenocarcinoma, signet-ring type of probable gastric origin, focal areas of intestinal metaplasia	Died 2 years, 11 months
Stoma	Polypoid adenocarcinoma obstructing the afferent loop with diffuse metastasis	Died 1 year, 3 months
Stoma	Extensive adenocarcinoma, grade IV, about the stoma, infiltrating all layers	Died 2 months
Stoma	Extensive gelatinous adenocarcinoma with metastasis to liver involving the gastroenterostomy stoma	Died 11 months
Lesser curvature and pylorus	Extensive adenocarcinoma	Without evidence of cancer 2 years
Cardia	Extensive adenocarcinoma of the promixal portion of remaining stomach	Living with cancer
Stoma	Extensive signet-ring adenocarcinoma encircling the stoma, not obstructing the stoma	Living with cancer

A. *B.*

Fig. 2.—*A*, Parastomal cancer developing in residual stomach after partial gastrectomy for peptic ulcer. *B*, Parastomal cancer developing in residual stomach after partial gastrectomy for peptic ulcer.

Fig. 3.—Multicentric gastric cancers developing late after gastroenterostomy for peptic ulcer.

Location of the Subsequent Tumor in the Stomach.—Thirteen of our 19 patients (86.4 per cent) had gastric cancer compromising or developing at the site of the gastrojejunal stoma. Four patients (21 per cent) developed the primary cancer in the region of the cardia. In one patient the cancer was definitely prepyloric in origin, and in one patient the cancer involved so much of the stomach in its generalized distribution that the surgeon was unable to ascertain in which particular segment of the stomach the neoplasm originated. The frequency of development in the neighborhood of the stoma may have important etiologic implications. However, it has long been known that the antrum and corpus of the stomach are frequent sites for the spontaneous development of cancer; therefore too much importance must not be placed upon the coincidence of the juxtaposition of the cancer to the pre-existing stoma, inasmuch as this portion of the stomach is the part most commonly employed for the construction of a gastrojejunostomy.

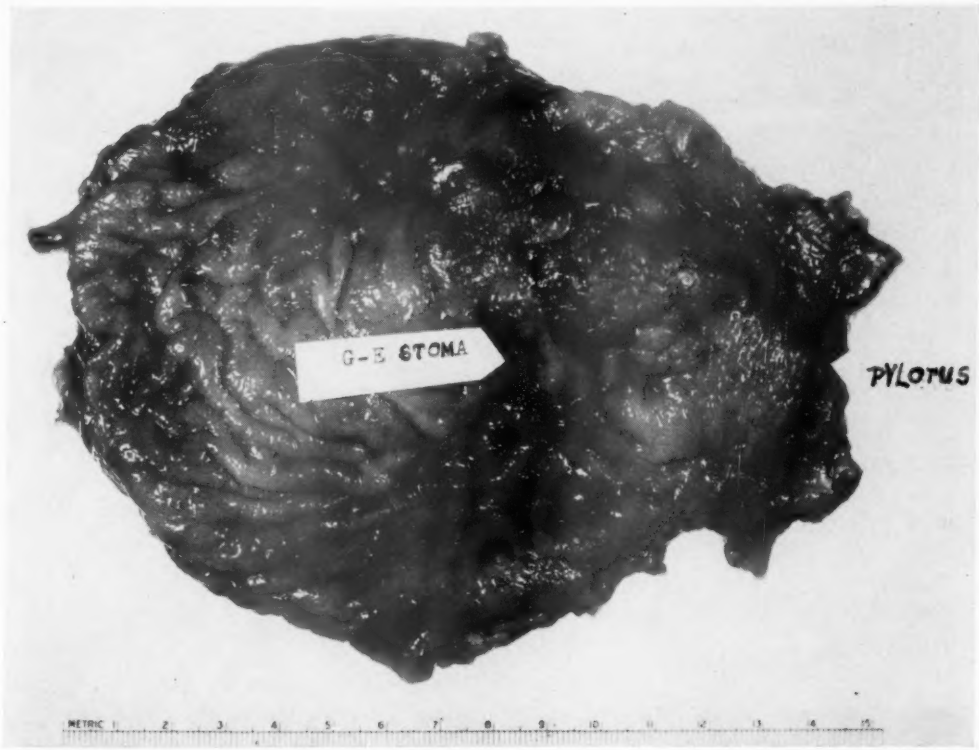
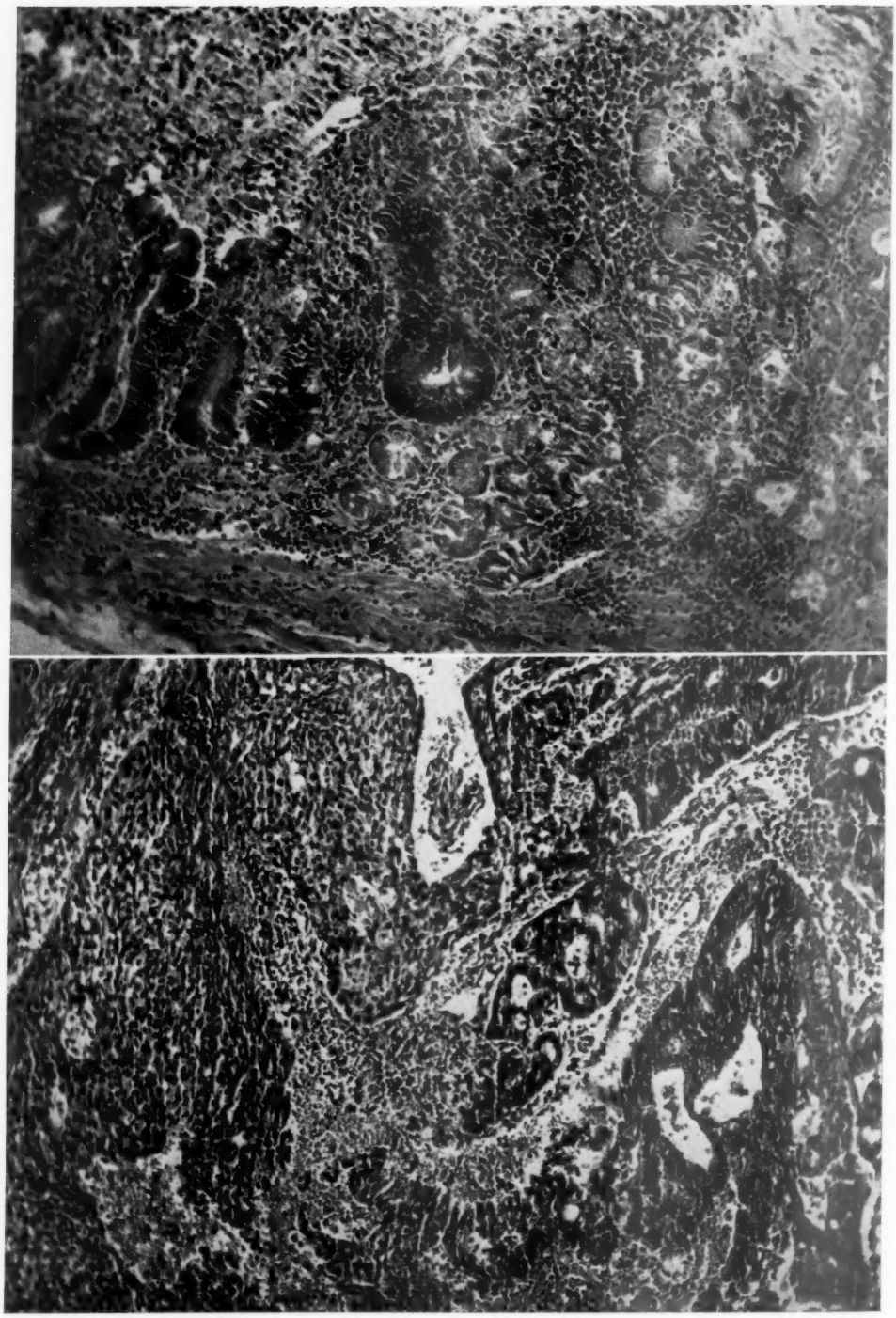


Fig. 4.—Subtotal gastrectomy for cancer developing on margin of gastroenterostomy stoma.

Etiologic Considerations.—It is not possible to prove that the late development of gastric cancer in these patients is due either to any etiologic relationship with the previous disease such as a duodenal or gastric ulcer or to a specific predisposition of the residual stomach with a new gastrointestinal stoma to undergo neoplastic changes. However, it is a certainty that at some time during the postoperative period, 75 per cent of patients undergoing gastroenterostomy will experience some manifestation of the so-called "gastroenterostomy disease" which may be transitory or intermittent. This complication

A.



B.

Fig. 5.—*A*, Intestinal-type metaplasia in parastomal gastric mucosa of patient bearing adenocarcinoma of stomach. *B*, Epidermoid metaplasia in parastomal mucosa of patient having combined epidermoid carcinoma and adenocarcinoma of stomach.

is characterized by acute inflammatory changes in the gastric mucosa immediately surrounding the new stoma; such changes as redness, edema, and minute superficial erosions, pseudopolypoid excrescences, membranous exudate, and microscopic evidence of gastric mucosal atrophy. The precipitant exposure of the parastomal gastric mucosa to the alkaline tide of bile and pancreatic juice is conceivably a potent irritating factor. The benign marginal ulcers characteristically develop on the jejunal side of the stoma, and the carcinomatous lesions occur solely on the gastric side.

Symptomatology and Diagnosis.—The diagnostic recognition of the supervention of gastric cancer after gastroenterostomy or subtotal gastrectomy for peptic ulcer is usually delayed because two-thirds of these patients are treated by expectant conservative therapy due to the memory of the benignity of the original disease for which the initial operation was performed. The common mistake is to assume that subsequent signs and symptoms are indicative of a recurrence of the original ailment. The patients and physicians initially consulted commit this grievous error.

In the presence of a gastroenterostomy it is a difficult radiographic diagnostic feat to detect the presence of cancer in the distal gastric segment. The radiographic interpretation of such films has been incorrect in 50 per cent of the initial studies. The x-ray examination should be made in the Trendelenburg position in order to avoid rapid emptying of the stomach.

The gastroscope finds a useful place in the procedures necessary to establish the differential diagnosis between carcinoma in the residual stomach and a benign nonneoplastic or inflammatory disease. Polypoid tumors and ulcers with necrotic bases may be correctly interpreted as being cancer on gastroscopic visualization. Gastric analysis in our experience has offered little as a supplementary aid because of the ebb and flow of intestinal juices through the patent stoma.

Although cytologic studies of the gastric aspirate have not been employed in these reported cases, it is our afterthought that perhaps it may be of great future value in the establishment of a correct differential diagnosis.

Pathologic Anatomy of the Tumor and the Gastric Mucosa.—The majority of the gastric carcinomas developing after gastroenterostomy or partial gastrectomy have been polypoid or mixed ulcerative and polypoid in their gross anatomic types. Metaplastic mucosal changes were observed in 26 per cent of these patients predominantly within the mucosa adjacent to the gastroenterostomy stoma. The metaplastic changes were chiefly of the intestinal type and have been interpreted as a manifestation of regenerative mucosal changes after irritation and erosion rather than of development from congenital arrests. In one remarkable case we found epidermoid metaplasia of the gastric mucosa in the same patient who had a combined epidermoid carcinoma and adenocarcinoma of the gastroenterostomy stoma; perigastric lymph nodes in this patient contained metastatic deposits only of the adenocarcinoma moiety. It has been our experience that gastric mucosal metaplasia has been quite rare in patients with duodenal ulcer, not so infrequent in patients with gastric ulcer, and quite

common in stomachs bearing carcinoma in which instances the fundal mucosa is more commonly implicated. In our patients who suffered the late development of gastric cancer after gastroenterostomy or partial gastrectomy, the mucosal metaplasia seemed to be distributed in the neighborhood of the gastroenterostomy stoma.

Treatment of the Gastric Cancer.—In our group of patients developing gastric cancer after gastroenterostomy, only 7 (36.8 per cent) of the 19 patients had gastrectomies; of these 5 had total gastrectomies and 2 had extended total gastrectomies. The rate of resectability in this group as compared with that for cancers of the stomach as a whole in the Memorial Center series and over a 30-year period is comparable (33.9 per cent). The explanation of this low resectability rate lies, perhaps, in the fact that this is a small series and does not represent our recent experience but extends back to and including patients experiencing this complication since 1927. One unfortunate mistake made by us, and which is considered worthy of comment, was to perform a transthoracic vagotomy based upon the presumptive but incorrect diagnosis of marginal ulcer. The stoma defect in this patient later proved to be carcinomatous. Had the approach for the vagotomy been performed by the abdominal route, the true nature of the stomal defect would have been detected and a total gastrectomy might have been accomplished. We believe, therefore, that all surgical approaches for anticipated vagotomy for presumptive marginal ulcers should be by way of a laparotomy rather than by thoracotomy in order to ascertain the absence or presence of cancer at the stoma.

End Results of Therapy of These Gastric Cancers.—Only 3 of the 7 patients who underwent gastrectomy are living and well: one for 8 years, one for 2 years, and a third who was well at the end of 3 years before being lost to follow-up examination.

Inasmuch as the vast majority of marginal ulcers or benign stomal abnormalities evoking severe symptoms occur within the first 3 years following the initial gastroenterostomy or subtotal gastrectomy, the general rule might be followed that if any signs, symptoms, or x-ray evidence of malfunctioning, stenotic, or ulcerating lesions develop in the residual stomach after this 3-year period, these findings should be considered by the examining physician with a high index of suspicion of cancer.

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GASTROJEJUNAL ULCER PRESENTING AS A MASS IN THE ABDOMINAL WALL

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GASTROJEJUNAL ulcer has long tested the diagnostic skill of the internist, radiologist, and surgeon. In many cases the diagnosis is quite easily established by history, physical examination, and radiologic studies. However, in some cases it may be difficult to be certain of the diagnosis even at the time of abdominal exploration.

The manifestations or complications most frequently leading to the diagnosis of gastrojejunal or marginal ulcer are pain in 95 per cent, vomiting in 50 per cent, hemorrhage in 25 to 50, free perforation in 10, and gastrojejunocolic fistula in 10 to 15.[2, 4-6, 8, 11, 14-19] A less common complication of marginal ulcer is penetration of the anterior abdominal wall with formation of a palpable mass. In the American literature, mention of this complication is almost limited to the reports from the Lahey Clinic.[11, 12] In England, Garnett Wright[19] found 16 instances of anterior abdominal wall penetration in 458 marginal ulcers in his collective series of 1935.

In the past year 3 cases of gastrojejunal ulcer penetrating the anterior abdominal wall have been encountered at the Vanderbilt University Hospital and Thayer Veterans Administration Hospital. In all 3 instances a palpable left upper quadrant mass was present. These patients form the basis of this report.

CASE REPORTS

CASE 1.—A 44-year-old white man was admitted to Thayer Veterans Administration Hospital for the first time Oct. 3, 1956. He had been hospitalized elsewhere since 1944 with hebephrenic schizophrenia and a chronic duodenal ulcer. In 1952 an antecolic gastroenterostomy was performed for relief of pyloric stenosis. The patient was well until 1956 when weight loss and a left abdominal mass were noted. Physical examination revealed a poorly nourished, uncommunicative man in no distress. There was a left paramedian scar and lateral to this in the left upper quadrant there was a hard, nontender, 5 by 5 cm. mass within the abdominal wall. A gastrointestinal series was not performed. The mass was biopsied under general anesthesia. Frozen sections and paraffin sections of the biopsy specimen revealed scar tissue. The postoperative course was uneventful and the patient was returned to the referring hospital. One year later, Nov. 29, 1957, he was readmitted with recurrent weight loss, abdominal tenderness, and a left upper quadrant abdominal mass. Physical examination was essentially unchanged. An overnight gastric secretion collection revealed 40.8 mEq. of free acid. A gastrointestinal x-ray revealed a large marginal ulcer penetrating the anterior abdominal wall (Fig. 1). A barium enema revealed no

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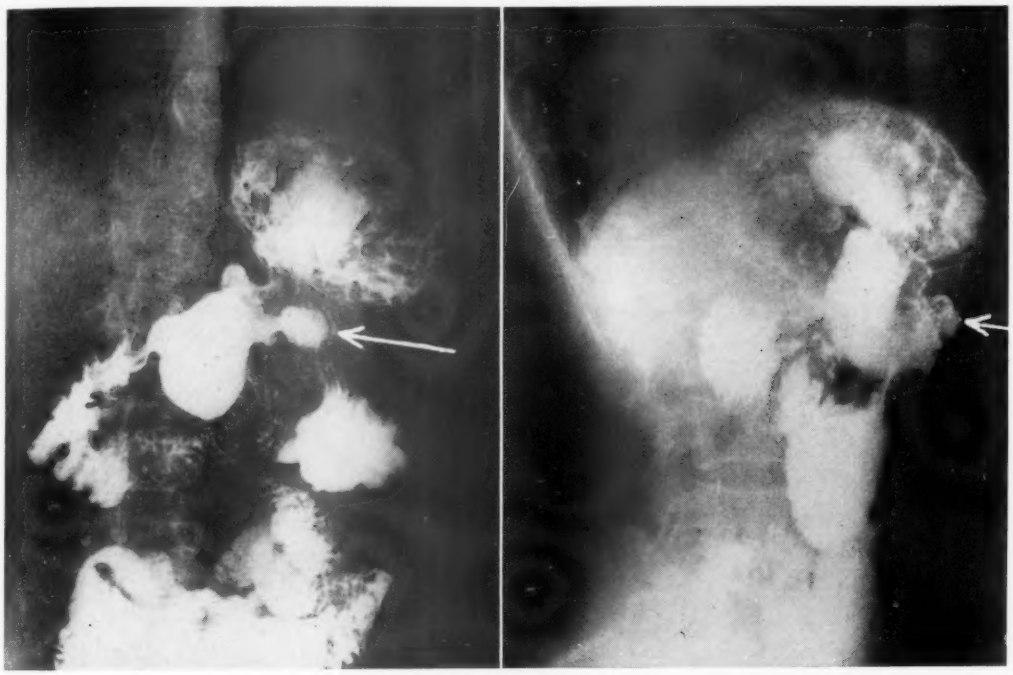
abnormality. On Dec. 20, 1957, abdominal exploration revealed the anastomotic site was adherent to the anterior abdominal wall with a large gastrojejunal ulcer which was deeply penetrating the rectus fascia and muscles. The mass consisted of a large ulcer crater and surrounding scar tissue. A hemigastrectomy, vagotomy, and Billroth I anastomosis were performed. Microscopic study revealed an acute marginal ulcer. The postoperative course was benign and the patient has continued to do well.



A. *B.*

Fig. 1.—*A* and *B*, Case 1. Gastrointestinal series revealing large gastrojejunal ulcer penetrating anterior abdominal wall.

CASE 2.—A 44-year-old white man had been admitted to Thayer Veterans Administration Hospital three times between 1946 and 1952 for treatment of an x-ray proved duodenal ulcer. In May, 1956, at another hospital he had undergone a partial gastrectomy with an antecolic Hofmeister anastomosis. The patient was well until December, 1957, when he noted the onset of left upper quadrant abdominal pain. Twelve days prior to admission he was hospitalized elsewhere with the presumptive diagnosis of left renal colic. This diagnosis was not proved, his pain persisted and he was transferred to Thayer Veterans Administration Hospital Jan. 3, 1958, for further evaluation. Antibiotics had been administered during the preceding week. Physical examination revealed a temperature of 99° F., pulse 100, and blood pressure 130/60. The patient was a poorly nourished white man weighing 95 pounds, in acute distress with abdominal pain. There was tenderness and muscle spasm in the left abdomen which extended around into the left flank and costovertebral angle. There was a hard, tender, 15 cm., discoid mass involving the left midabdomen and extending into the left flank. White blood count was 14,200. Urinalysis revealed no abnormality. A gastrointestinal series revealed irritability at the site of the gastroenterostomy, but a marginal ulcer could not be demonstrated. Shortly after admission his temperature rose to 101° F. and the abdominal tenderness and muscle spasm became generalized. An emergency abdominal exploration revealed obstruction of the afferent loop of the gastroenterostomy with early gangrene of the jejunal wall adjacent to the gastroenterostomy. There was a large gastrojejunal ulcer at the anastomotic site. This ulcer

had perforated through the peritoneum and posterior rectus fascia and had formed a large discoid abscess in the anterior abdominal wall. The abscess contained several hundred cubic centimeters of foul-smelling, purulent material and measured 12 cm. in diameter (Fig. 2). The gastrojejunostomy and 5 inches of jejunum on either side of the anastomosis were resected. A Billroth I anastomosis was performed and jejunal continuity was restored by an end-to-end enteroenterostomy. The abscess was drained through stab wounds in the left flank. Bacteriologic cultures revealed *Escherichia coli* and Proteus, sensitive to Chloromycetin. The early postoperative period was marked by dramatic improvement, but a wound infection and subsequently a duodenal fistula developed. After many efforts, a feeding tube was inserted through the fistula into the duodenum and the jejunum. It required several months to eradicate the infection and produce a weight gain from 90 to 103 pounds. The fistula persisted and 4 months after his first operation, abdominal exploration was again performed. The gastroduodenostomy was resected and an antecolic Hofmeister gastrojejunostomy was performed. Again in the postoperative period an enteric fistula became evident but this closed promptly with conservative measures. In June, 1958, small intestinal obstruction required lysis of adhesions. Since that time he has done well and attained a weight of 130 pounds.

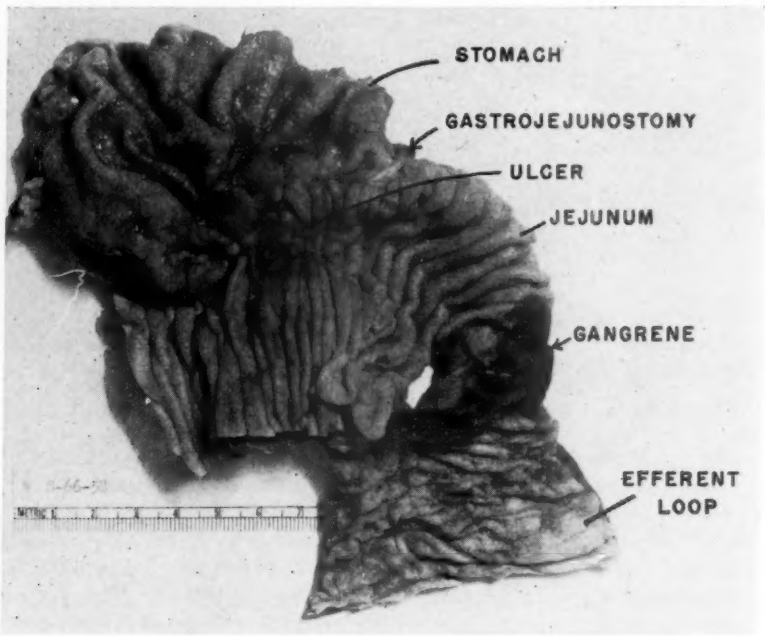


Fig. 2.—Case 2. Resected specimen revealing gastroenterostomy, marginal ulcer, and gangrene of afferent loop of jejunum. Defect in jejunal wall adjacent to area of gangrene is iatrogenic.

CASE 3.—A 48-year-old white man was admitted to Vanderbilt University Hospital for the first time on May 7, 1958, with a hard, tender left upper quadrant abdominal mass. Past history revealed evidence of a duodenal ulcer for 10 years. Three years prior to admission a gastroenterostomy was performed for pyloric stenosis. One year prior to admission he noted left abdominal pain and sustained a 30 pound weight loss in the ensuing 12 months. Two weeks prior to admission, he first noted tarry stools. On admission he was found to be a poorly nourished man in moderate distress with left abdominal pain. In the left upper quadrant of the abdominal wall there was a 3 by 3 cm., hard, tender mass. A gastrointestinal series revealed a marginal ulcer distal to the anastomosis (Fig. 3). Overnight gastric secretions revealed 50.4 mEq. of free acid. Abdominal exploration revealed an antecolic gastrojejunostomy with a large marginal ulcer penetrating the anterior abdominal

wall. There was no evidence of abscess formation. The gastroenterostomy was resected in continuity with a block of peritoneum and posterior rectus fascia. A hemigastrectomy, vagotomy, and antecolic Hofmeister anastomosis were performed. The postoperative course was benign and the patient has continued to do well.

DISCUSSION

In the first case, over a year elapsed from the time the patient was first seen until a definitive diagnosis was made and proper treatment effected. This patient's inability to communicate with his physicians undoubtedly compounded the difficulty in elucidating the problem. When a gastrointestinal x-ray was performed, the diagnosis was painfully apparent. Unfamiliarity with a marginal ulcer presenting as an anterior abdominal wall mass or abscess delayed recognition of the proper diagnosis in this patient, as well as in Case 2. Earlier

Fig. 3.—Gastrointestinal series revealing gastrojejunal ulcer.

recognition of the situation in the second patient with prompt drainage of the abscess and subsequent surgical management of his marginal ulcer would undoubtedly have avoided the many problems encountered. Gangrene of the afferent loop was a late complication of the marginal ulcer and abscess. The mimicry of left renal colic by marginal ulcer and abdominal wall abscess is noteworthy.

The first patient apparently withstood the ulcer penetration of the abdominal wall and if an abscess was ever present it had subsided. The second patient was in critical condition on admission and, after prolonged and extensive treatment, now seems to have made a good recovery. The third patient

seems to complete the spectrum that such patients may present. The penetration of the abdominal wall by the ulcer was at an early stage pathologically, and a minimum of difficulty attended an excellent recovery.

The paucity of experience in this clinic with abdominal wall mass or abscess as a manifestation of gastrojejunal ulcer has an apparent explanation in the type of gastroenterostomy usually performed or encountered (that is, posterior anastomosis). Gastrojejunocolic fistula is usually a complication associated with a retrocolic gastrojejunal anastomotic ulceration.[9, 11, 15, 17-19] The proximity of the ulcer to the colon is the apparent explanation. On the other hand, abdominal wall mass or abscess as a result of a marginal ulcer is associated with an antecolic gastrojejunal anastomosis.[8, 11, 12, 19] An antecolic gastrojejunostomy was present in each case of this report. This is also the case in all reported instances encountered in the literature, although it is difficult to be certain which type of gastroenterostomy was present in the 16 cases reported by Garnett Wright.[19] His discussion implies that an antecolic anastomosis was uniformly present. The performance of antecolic gastrojejunal anastomosis in treatment of both carcinoma and duodenal ulcer has long been advocated by the Lahey Clinic.[7] Reported series of marginal ulcer from this clinic invariably mention abdominal wall penetration as one of the complications encountered.[11, 12] In 1948 Lowden of Edinburgh[8] in a discussion of marginal ulcer states, "The development of an abscess in the anterior abdominal wall was previously a common event in these cases, but it is now rarely seen because the anterior anastomosis is seldom performed."

If a gastrojejunocolic fistula is more likely to occur with a retrocolic anastomosis and an abdominal wall abscess is more likely to follow an antecolic anastomosis, should this influence the surgeon's choice of procedure? Of these two complications the gastrojejunocolic fistula would seem the least desirable. The mortality rate associated with treatment of gastrojejunocolic fistula would seem more formidable.[9, 15, 17, 18] However, there seems to be little available data on treatment of marginal ulcer with abdominal wall abscess. In the past, the preponderance of opinion favored posterior anastomosis as less likely to result in marginal ulceration.[8-10, 14, 17-19] However the less numerous but no less authoritative advocates of anterior anastomosis have disagreed with this point of view.[7, 11, 12] Substantiating proof for either point of view is still lacking. The true incidence of gastrojejunal ulcer is indeed difficult to obtain. The addition of vagotomy and repopularization of the Billroth I anastomosis have added two more variables. Recent series of hemigastrectomy plus vagotomy in the treatment of duodenal ulcer seem to have reduced the incidence of marginal ulcer to an exceedingly low point[1, 3]; however, a truly long-term follow-up will be required to confirm or refute this impression. Vagotomy was performed in the first and last patients in this report and would have been performed in the second patient if there had not been apprehension concerning mediastinal spread of pre-existing intra-abdominal infection. If evidence of recurrent marginal ulceration develops in this patient a transthoracic vagotomy will probably be performed.

CONCLUSION

A patient presenting with a left upper quadrant abdominal mass and a past history of gastric surgery for duodenal ulcer may well have a gastrojejunal ulcer which has penetrated the anterior abdominal wall. If such a marginal ulcer exists, the primary operation almost assuredly involved an antecolic gastrojejunal anastomosis.

SUMMARY

Three cases of gastrojejunal ulcer which penetrated the anterior abdominal wall with the formation of a mass or abscess have been presented.

In each case an antecolic gastrojejunostomy had previously been performed in the treatment of duodenal ulcer. In one patient partial gastrectomy had been included in the original operation.

The factors concerned in the production of this complication have been discussed.

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THE BILLROTH I AND BILLROTH II RECONSTRUCTIONS

A Clinical Comparison of Results of the Two Methods

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THE Billroth I type reconstruction following gastric resection enjoyed a brief period of popularity following its introduction in 1881.[2, 11] The procedure was then largely abandoned due to technical difficulties which resulted in an increasing number of postoperative complications. During the past 10 to 15 years, however, a renewed interest in the Billroth I reconstruction has been manifested by an increased number of reports appearing in the surgical literature.[6, 10, 12-14] This, no doubt, stems from the fact that surgeons have not been entirely satisfied with the results following the conventional Billroth II type of reconstruction or one of its modifications. At present, there exists considerable divergence of opinion in regard to the relative merits of the Billroth I versus the Billroth II type reconstruction following subtotal gastric resection.[1, 3, 4, 7-9, 16-18]

This study serves as a clinical evaluation of results of two groups of patients with benign gastric and duodenal ulcer disease. One group underwent gastric resection with establishment of continuity using an end-to-end gastroduodenostomy (Billroth I), and the other group was subjected to subtotal gastric resection with a conventional Billroth II type of reconstruction or one of its modifications. *Each patient in both groups with duodenal ulcer underwent bilateral subdiaphragmatic vagotomy in addition to resection.* The resection in the duodenal ulcer cases consisted of removal of the gastric antrum, which encompassed an estimated 40 to 50 per cent distal gastrectomy. Vagotomy was not employed as an adjunct to resection in patients with gastric ulcer.

An attempt has been made to compare the two groups of patients in regard to operative mortality, hospital complications, postoperative weight status, anemia, and incidence of postprandial symptoms. An appraisal of the results obtained from each operation has also been made. An additional purpose of the study has been to determine, if possible, the relative indications for the selection of either the Billroth I or Billroth II reconstruction for the particular patient with a benign gastric or duodenal ulcer.

CLINICAL MATERIAL

The Billroth I group consists of a total of 107 patients, with a postoperative follow-up study ranging from 6 months to 3½ years. Ninety-eight of this number were operated upon for duodenal ulcer and 9 patients underwent operation for a benign gastric ulcer. In the doudenal ulcer group, there were 70 men and

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28 women. The ages ranged from 22 to 77 years, with an average age of 48 years. Among the gastric ulcer patients, there were 5 women and 4 men, with the average age at time of operation being 52 years.

The Billroth II series comprised a total of 209 patients followed for a minimum of 6 months to 11½ years. One hundred and ninety-six patients were suffering from complications of duodenal ulcer and 13 patients had a benign gastric ulcer. In the duodenal ulcer group, there were 172 men and 24 women, whose ages ranged from 21 to 77 years, with an average age of 49 years. The gastric ulcer patients comprised 7 men and 6 women, who averaged 52 years of age (Table I).

TABLE I

NUMBER OF PATIENTS	DUODENAL ULCER		GASTRIC ULCER	
	MEN	WOMEN	MEN	WOMEN
	Billroth I			
107	70	28	4	5
	Average age 48 years		Average age 52 years	
	Billroth II			
209	172	24	7	6
	Average age 49 years		Average age 52 years	

The postoperative hospital stay among the Billroth I group averaged 9 days and, in the Billroth II group, 9.1 days.

Mortality.—Among the 107 patients undergoing a Billroth I reconstruction, there were 3 hospital deaths (mortality 2.8 per cent). In the Billroth II cases, there were 8 deaths (mortality 4 per cent) among 209 patients. In addition, there were 8 patients in this latter group lost to follow-up (Table II).

TABLE II

	MORTALITY	MORTALITY RATE	LOST TO FOLLOW-UP	PATIENTS FOLLOWED
Billroth I				
107 patients	3	2.8%	0	104
Billroth II				
209 patients	8	4.0%	8	193

Two of the 3 deaths in the Billroth I group occurred in elderly men undergoing surgery for duodenal ulcer. One was a 68-year-old man, who developed small bowel obstruction in the postoperative period. The obstruction occurred at the site of a temporary gastrostomy which had been used as a substitute for nasogastric suction. He was re-explored and the obstruction released, but while he was on the operating table cardiac arrest ensued which failed to respond to resuscitative measures. The second death in the duodenal ulcer group occurred in a 74-year-old man with hypertension, who was operated upon after a third massive hemorrhage. He developed irreversible hypotension and vascular collapse during the early postoperative period. The third death occurred in an 80-year-old diabetic woman, who underwent an apparently uneventful postoperative course following an emergency gastric resection for a bleeding superficial benign pyloric ulcer. She re-entered the hospital 3 weeks following discharge with a severe wound infection and the diabetes presented a problem to

control. While under observation, she developed a rapidly exsanguinating hemorrhage and, at post mortem, was found to have a superficial ulcer in the residual gastric pouch which proved to be the source of the fatal bleeding. It was felt that this ulceration probably resulted from a stress reaction. None of the 3 deaths were directly attributable to a technical difficulty resulting from the performance of the Billroth I type reconstruction.

In the Billroth II group, the 8 deaths occurred among patients with duodenal ulcer. No deaths took place in the small group of 13 patients operated upon for gastric ulcer. Five deaths occurred in poor-risk patients undergoing surgery for pyloric obstruction. Two of the 5 patients were suffering from pre-existing cardiac disease and died during the postoperative course as a result of cerebral hemorrhage and left ventricular failure, respectively. The third patient with pyloric obstruction had associated tabes dorsalis and succumbed to a pulmonary embolism. A fourth patient with associated nephrosclerosis died of renal failure. The fifth death occurred in an elderly woman who developed stomal obstruction postoperatively. Despite two attempts at stomal revision, she continued to do poorly and expired of emaciation and vascular collapse. In addition, there were 3 patients operated upon as emergencies for massive hemorrhage who also expired. In one of these, death was due to postoperative bleeding from an ulcer site low in the duodenum, which had not been properly cared for at the time of operation. One patient died of mediastinal emphysema and another from a massive pulmonary embolus.

Thus, among the 8 deaths, only one could be directly attributable to a technical error in the performance of the Billroth II reconstruction.

Postoperative Complications.—In the Billroth I cases, inclusive of hospital deaths, there was a total of 21 significant complications occurring among 20 patients (over-all complication rate of 19 per cent). In the Billroth II group, the over-all complication rate, including deaths, likewise total 19 per cent (38 complications among 36 patients). The complications encountered in both groups of patients may conveniently be separated into those occurring as a direct result of a technical error in the performance of the particular operative reconstruction and those which are commonly associated with any major surgical procedure in general.

In the Billroth I group comprising 107 patients, obstruction at the gastroduodenostomy stoma was the most frequently encountered complication resulting from a technical fault. It occurred in 7 patients (6.5 per cent) during the postoperative period and necessitated reoperation in 5 of the 7. In 6 of the 7 patients, obstruction became apparent during the early postoperative course. In one patient, symptoms of obstruction first became manifest 3 months after operation. A gastrointestinal series performed on this patient demonstrated a deformity on the anterosuperior aspect of the duodenum near the site of the anastomosis, which was interpreted by the radiologist as suggestive of a recurrent ulceration (Fig. 1). However, the patient had noted no abdominal pain during this 3-month interval and free HCL was absent from the gastric pouch. In

addition, the insulin test was negative and pH studies of the gastric juice approached neutral readings. At reoperation, an adhesive band extending from the superior surface of the duodenum to the inferior border of the right lobe of the liver was responsible for producing a kink and angulation at the anastomotic site. In 4 patients, stomal difficulty was corrected by either a Heineke-Mikulicz plastic procedure or else simple gastroenterostomy. In 2 patients, the delayed emptying responded to prolonged nasogastric suction.

There were 8 patients (3.8 per cent) that developed stomal obstruction among the group of 209 patients who underwent a Billroth II reconstruction. In 5 of this group, prolonged gastric suction was successful in alleviating the obstruction. One patient later succumbed, as mentioned before, and stomal revision ultimately became necessary in 2 instances.

Fig. 1.—Deformity on the anterosuperior aspect of the duodenum near the site of anastomosis *(arrow)*, which was interpreted by the radiologist as suggestive of a recurrent ulceration.

Postoperative hemorrhage serious enough to merit concern was noted in 3 patients (2.8 per cent) among the Billroth I group. In 2 instances, the bleeding apparently came from a fresh suture line and responded to transfusion therapy. The other bleeding episode occurred in an elderly woman who underwent resection 3 weeks prior for a benign gastric lesion, as previously mentioned.

There were only 2 postoperative bleeding episodes encountered among the Billroth II group (0.9 per cent) and one of these proved fatal, as described elsewhere. A bleeding suture line was apparently responsible for the other bleeding episode and this ceased spontaneously.

A leak at the anastomotic site was noted in one patient (0.9 per cent) in the Billroth I group and this complication did not prove fatal. A leak from the duodenal stump occurred in only 3 patients (1.4 per cent) in the Billroth II group. In each case, the fistula closed spontaneously.

There was no instance of an injury inflicted to the common bile duct in either group of patients. There was, however, one case of transient icterus among one of the patients in the Billroth II group who developed stomal obstruction. It was felt that, no doubt, considerable edema and induration in the vicinity of the closed duodenal stump and head of the pancreas accounted for the rise in bilirubin, since some trauma was inflicted to the head of the pancreas in removing an adherent posterior wall ulcer.

In the Billroth I series, there was one case in which the transverse colon was injured inadvertently in dividing adhesions between the duodenum and colon. A fecal fistula resulted which later necessitated surgical closure.

Postoperative acute pancreatitis has been cited as a rather frequently encountered complication following gastric resection for duodenal ulcer and, as a rule, is more common in patients undergoing a Billroth II reconstruction. It is interesting to note that not a single instance of pancreatitis was diagnosed in the 2 groups of patients under consideration, but admittedly the milder forms of the disease could have existed undetected. We were ever cognizant of this complication, however, during the postoperative period. Serum amylase determinations were performed on many patients in both groups, usually daily for a period of several days following operation. On occasion, particularly where there was difficulty encountered in removing an adherent posterior wall ulcer, there occurred a rise in the serum amylase, usually for a 24- to 72-hour period. This was detected more often in the Billroth II group, as this type of reconstruction was usually employed in dealing with the more difficult cases of duodenal ulcer. A rise in amylase was not associated with the clinical picture of acute pancreatitis in this group of patients.

TABLE III. POSTOPERATIVE COMPLICATIONS INCLUDING HOSPITAL DEATHS

NUMBER	BILLROTH I	NUMBER	BILLROTH II
7	Stomal obstruction (6.5%)	8	Stomal obstruction (3.8%)
3	Postoperative hemorrhage (2.8%)	2	Postoperative hemorrhage (0.9%)
1	Anastomotic leak (0.9%)	3	Leaking stump (1.4%)
1	Fecal fistula (0.9%)	1	Postoperative icterus (0.9%)
2	Bronchopneumonia	2	Bronchopneumonia
2	Wound disruptions	4	Atelectasis
1	Tracheobronchitis	4	Wound disruptions
1	Enterocolitis	2	Wound infections
1	Cardiac arrest	1	Enterocolitis
1	Vascular collapse		
1	Acute prostatitis	8	Vascular complications { peripheral, cerebral, pulmonary
		1	Postoperative psychosis
		1	Renal failure
		1	Mediastinal emphysema
21		38	

Among the complications not related directly to the particular type gastric reconstruction, vascular complications were encountered most frequently. The fact that they all occurred in the Billroth II group was probably coincidental. Bronchial pneumonia, atelectasis, and wound dehiscence were complications common among both groups. The remaining complications were, for the most part, quite similar in each group and represented the ones usually encountered with any major abdominal procedure (Table III).

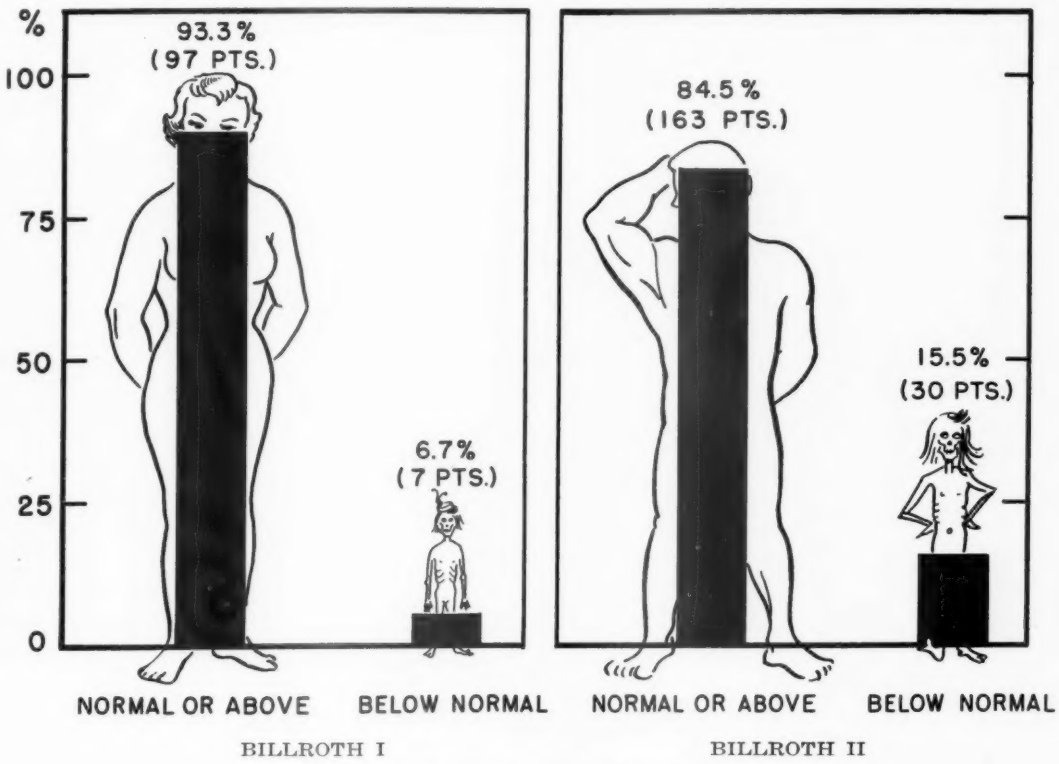

Fig. 2.—Postoperative weight status.

Weight Status.—An assessment of the postoperative weight status has been made on the 104 patients comprising the Billroth I group followed 6 months to 3½ years. Only 7 patients (6.7 per cent) have lost weight since undergoing operation. Weight loss was not excessive in any instance and has varied from 10 to 20 pounds. Five of the 7 patients who lost weight were women. Each patient showing a weight loss was operated upon originally for duodenal ulcer. None of the 9 patients undergoing resection for gastric ulcer have shown a postoperative weight loss. It is of interest in this regard that 3 patients in the gastric ulcer group underwent resections varying in extent from 75 to 90 per cent for high-lying giant gastric lesions.

In the Billroth II group, 193 patients have been followed for periods extending to 11½ years. Of that number, 30 (15.5 per cent) have lost weight varying in amount from 10 to 40 pounds. Twenty-seven of these patients were operated upon for duodenal ulcer and 3 for benign gastric ulcer. The 3 patients in the latter group were subjected to resection varying in extent from 60 to 75

per cent. Eight of the patients showing weight loss in the duodenal ulcer group were women and 19 were men. Further analysis shows that 21 of the 30 patients had difficulty maintaining ideal weight prior to operation and, in general, were of a slender build. Although the percentage of patients in the Billroth II group showing evidence of weight loss exceeded that in the Billroth I group, the weight loss in the former group by no means approaches the weight loss reported in most series following radical resections of the Billroth II type for duodenal ulcer. No doubt, the conservative resection and vagotomy performed in the present series for duodenal ulcer is responsible for the relatively small number of patients demonstrating actual weight losses. (Fig. 2.)

Anemia.—Anemia was encountered very infrequently in both groups of patients. Only one patient in the Billroth I series developed anemia during the follow-up period. This occurred in a woman undergoing vagotomy and antral resection for duodenal ulcer. There was no anemia among the 3 patients in the Billroth I group undergoing an extensive gastrectomy for a high-lying gastric ulcer.

In the Billroth II group, there were only 2 patients among the duodenal ulcer patients who developed postoperative anemia. Two of the patients in the gastric ulcer series undergoing 75 per cent resection likewise developed anemia which responded to iron therapy.

Dumping Syndrome.—Symptoms typifying the dumping syndrome were divided into those which were mild in character and, in many instances, transient. On occasions, mild dumping could be elicited only on careful questioning of the patient and usually the nature of the symptoms were such that they in no way interfered with the patient's well-being. Dumping was considered moderate in degree when it was of major concern to the patient and physician but did not interfere with the patient's pursuing a livelihood. This type of patient could usually be improved with instructive measures. Symptoms were graded severe when the patient was partially or totally handicapped as a result of the symptomatology.

Among the 104 patients with a Billroth I reconstruction, symptoms suggestive of dumping were noted in 23 per cent (24 patients). The symptomatology was mild in 18 patients (17 per cent). For the most part, it was transitory in nature and disappeared as a rule in several weeks to months. In 6 patients (6 per cent), the dumping was considered moderate in degree. Three of these patients were middle-aged women with various psychosomatic complaints. It is important to note that there were no cases of severe dumping in this group of patients. All but one of the "dumpers" represented patients operated upon for duodenal ulcer.

In the Billroth II group of 193 patients, the over-all incidence of dumping was 37 per cent (72 patients). Mild dumping occurred in 50 patients (26 per cent). In addition, moderate dumping was noted in 17 patients (9 per cent). In 5 patients (2 per cent), symptoms were of a severe nature (Fig. 3). Two patients in the latter category were totally incapacitated and each required reoperation with conversion of the Billroth II reconstruction to a Billroth I. Both

have now gained weight and have become symptom-free. Seven of the 13 patients in the gastric ulcer group complained of dumping and symptoms were of moderate severity in 4 of the 7 patients.

Recurrent Ulcer.—In the patients undergoing a Billroth I reconstruction, the follow-up period extending to 3½ years has not been sufficient to determine recurrence rates. However, in the light of a preliminary survey, it is of some interest to observe that only one recurrence has been found among the patients operated upon for duodenal ulcer. Approximately 70 of the 96 patients with duodenal ulcer have been followed from over 1 to 3½ years. The one recurrence took place in an elderly woman who re-entered the hospital 6 months after undergoing vagotomy and a 50 per cent resection. She was bleeding massively from a large posterior ulceration just distal to the gastroduodenostomy. A re-resection was performed, but due to her precarious state the periesophageal area

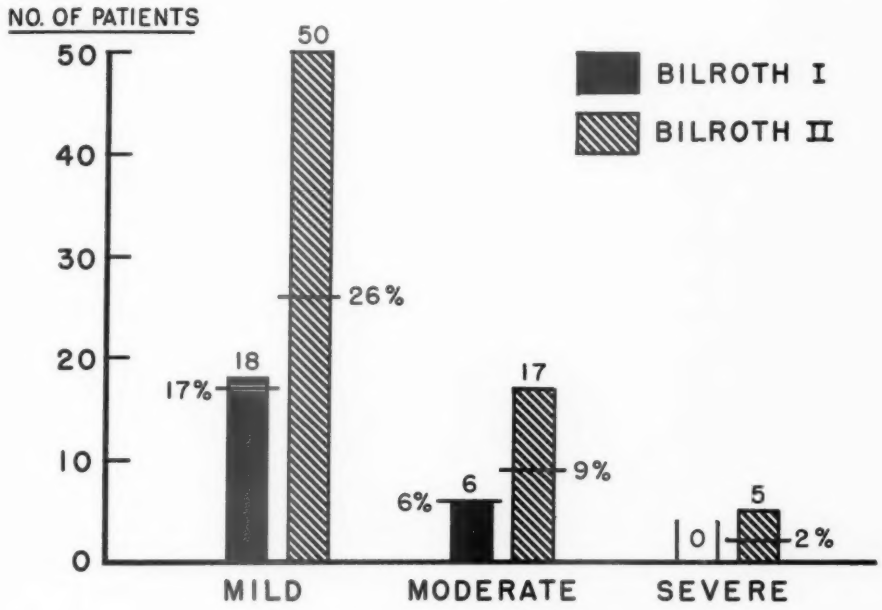

Fig. 3.—Dumping symptoms.

was not explored for a possible overlooked vagal fiber. Among the 9 cases in the gastric ulcer group undergoing a Billroth I reconstruction, there was the one patient cited under the mortality studies who re-entered the hospital 3 weeks postoperatively, bleeding from an ulceration in the gastric pouch. It was felt that this ulcer did not represent true peptic ulcer disease, but rather a stress phenomenon. The other possibility was that the ulceration could have been overlooked at the time of the original surgery. If this latter case is included, however, the recurrence rate is 1.9 per cent among 105 patients followed over this brief interval. There has been no instance of a suspected ulceration in the remaining 103 patients.

In the Billroth II group totaling 193 cases, there has been no instance of a suspected or proved recurrence among 180 patients undergoing a vagotomy and antral resection for duodenal ulcer with a follow-up period extending to 11½

years. This observation is becoming of increasing importance. Among 13 patients undergoing resection with a Billroth II reconstruction for gastric ulcer, there has been one recurrence. Thus, the over-all recurrence rate at present totals 0.5 per cent. (Table IV.)

TABLE IV. RECURRENT ULCERATION

NUMBER OF PATIENTS	DUODENAL ULCER RECURRENCE	GASTRIC ULCER RECURRENCE	RECURRENCE RATE
	Billroth I		
105	1	1*	1.9%
	Billroth II		
193	0	1	0.5%

*The one patient listed as a recurrence under gastric ulcer represents the patient who bled 3 weeks postoperative and expired.

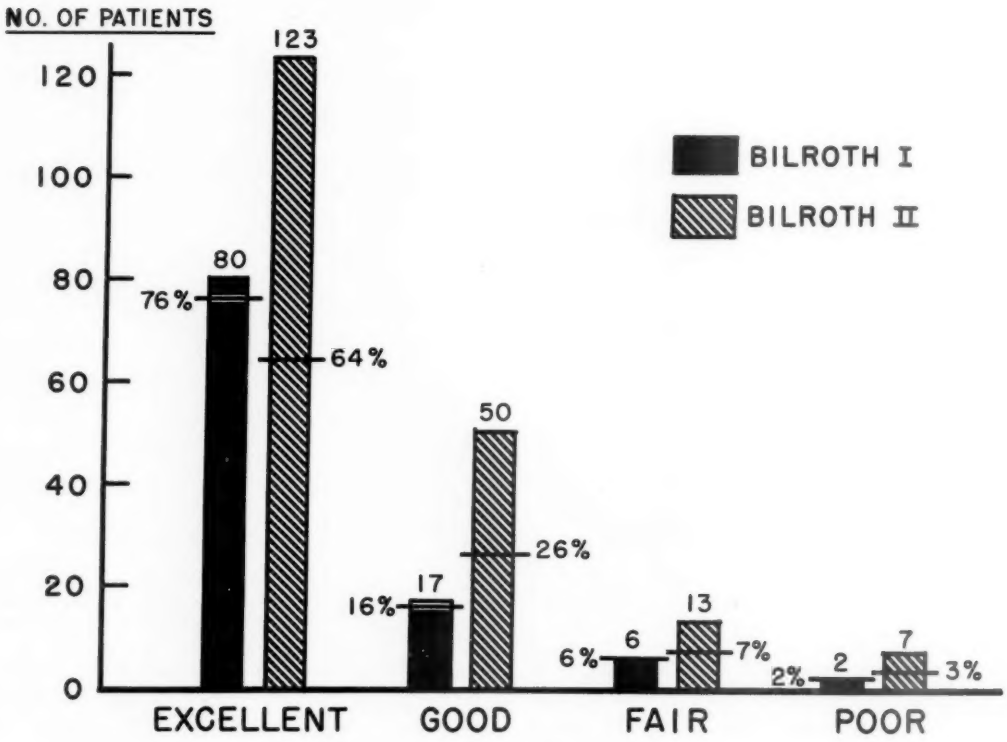

Fig. 4.—Results.

Results.—The results were graded as excellent for only those patients experiencing entire freedom from any gastrointestinal complaint. If minor intestinal disturbances were noted, such as transient fullness after meals, mild dumping symptoms, or occasional diarrhea, the result was listed as good. If the dumping was moderate in severity, if significant gastrointestinal disturbance was experienced, and if appreciable weight loss was noted, the result was classified as fair. If the patient had not received substantial benefit from the operation or if there was suggestion of a suspected or proved recurrence, the result was termed poor.

There were 80 patients (76 per cent) among the Billroth I group who obtained an excellent result from operation. Seventeen patients (16 per cent) were classified as good results, since their postoperative complaints are minimal and usually transitory. Six patients (6 per cent) were improved over their preoperative status but were considered as having obtained only a fair result. Poor results in 2 patients (2 per cent) are represented by the 68-year-old woman with the recurrent ulcer and the 80-year-old woman who bled 3 weeks after surgery possibly from a stress ulceration developing in the gastric pouch.

The results of the Billroth II cases show that 123 patients (64 per cent) have remainded symptom-free; 50 patients (26 per cent) have obtained a good result; and 13 patients (7 per cent) are graded as improved over their preoperative status, but the result is only fair. Seven patients (3 per cent) have obtained a poor result (Fig. 4). The latter category includes the one recurrence in the gastric ulcer group and the 2 patients with severe dumping who underwent reoperation. The remaining 4 patients listed as failures were women. It is of interest that 7 of the 13 patients obtaining a fair result were likewise women.

DISCUSSION

The difference in mortality rate of 2.8 and 4 per cent, respectively, among the present Billroth I and Billroth II groups is not of statistical significance. Of the 3 deaths in the Billroth I series, none could be directly attributable to a technical fault in performance of the gastroduodenal reconstruction. A mortality of 4 per cent among the Billroth II group is higher than that reported in some series, but it should be stressed that all 8 deaths occurred in poor-risk patients with coexistent disease in which operation was mandatory in each instance. As mentioned, one of these deaths was directly attributable to a technical difficulty in performance of the Billroth II anastomosis, and another death may possibly have been avoided if the bleeding from a retrobulbar ulcer had been more securely controlled.

The over-all complication rate of 19 per cent was equal in the 2 groups of patients. Stomal obstruction appeared to be the most frequently encountered complication common to both groups. It was manifest in a higher percentage of patients in the Billroth I group, being encountered in 7 of 107 patients (6.5 per cent), as compared to 8 patients (3.8 per cent) among the 209 comprising the Billroth II group. One of the 7 patients developing postoperative obstruction in the Billroth I group represented the first patient in the series who underwent gastroduodenostomy and a technical error accounted for this complication. In 5 cases, a large posterior penetrating duodenal ulcer was present and the duodenal tissue utilized in performing the gastroduodenal anastomosis was edematous and scarred and the entire ulcer could not be completely removed. Each of these cases represented an error in judgment, as a Billroth II type of reconstruction should have been utilized under the circumstances. The remaining patient presented a unique complication in our experience in developing stomal obstruction 3 months postoperatively on the basis of an extrinsic adhesive

band. Woodward[19] has mentioned obstruction at the gastroduodenal site occurring in the late follow-up period as a result of fibrotic narrowing at the anastomosis.

As a result of this experience, we have been careful in our selection of patients for a Billroth I reconstruction. We feel that the procedure is definitely contraindicated when operating upon a large posterior wall duodenal ulcer with considerable scarring, in which a normal 1 to 1.5 cm. cuff of duodenum cannot be mobilized distal to the ulcer site. It should be mentioned, however, that the decision to perform a Billroth I or Billroth II reconstruction is not made immediately when the ulcer is first visualized and palpated. In our experience, many posterior wall ulcers can be dissected from the pancreas with a minimum of operative manipulation and trauma. It is only after the ulcer has been completely exposed, its relation to the common duct ascertained, and the relative amount of local tissue reaction taken into account that a choice of the type of reconstruction is usually decided upon.

In Wallensten's series,[15] postoperative hemorrhage was a feature in 13 cases (1.5 per cent) among the Billroth II group; whereas this complication occurred in only 0.6 per cent of the Billroth I group. In the present series, the incidence of this complication was not significantly different among the 2 groups.

A leaking duodenal stump was noted in 3 patients among the Billroth II group, and only one patient in the Billroth I group showed clinical evidence of a leak at the gastroduodenal anastomosis. This latter case was that of a large, obese man, who developed abdominal pain, fever, and tachycardia on the fifth postoperative day. Subsequently, wound tenderness developed and an abcess was drained which was productive of bile-stained material. The fistula, however, closed promptly and no further difficulty ensued. In this particular patient, a normal cuff of duodenum was developed below the ulcer site at the time of operation, but the anastomosis was performed with difficulty in the depth of the upper abdomen. Even kocherization of the duodenum in an individual of this type build does not always provide the necessary exposure for an accurate gastroduodenal anastomosis. As experience has accumulated, it has become our policy when operating upon the large, obese patient with an increased anteroposterior diameter of the upper abdomen to perform a Billroth II reconstruction rather than attempt an end-to-end gastroduodenostomy.

Injuries to the common bile duct were not encountered in the present series. Wallensten states that this complication is seen more often following a Billroth II reconstruction, since probably the more difficult duodenal ulcers are operated upon by this method. Clinical evidence of acute pancreatitis was likewise absent from the list of postoperative complications in our patients. Observers have more often cited this drastic complication following a Billroth II reconstruction. Wallensten could not explain its occurrence on the basis of selection of patients in his series but felt the probable cause to be a stagnation of duodenal contents in the afferent jejunal limb with reflux of contents into the pancreatic ductal system.

Weight loss and nutritional disturbances have been observed to follow the Billroth II reconstruction more often than the Billroth I. This has been borne out both experimentally[5] and clinically. Weight loss was experienced in only 6.7 per cent of the Billroth I group under consideration and was noted in 15.5 per cent of the Billroth II group. The amount of weight loss among the individuals undergoing a Billroth I reconstruction was usually less than that experienced by a patient operated upon by the Billroth II method, since some of the latter patients lost 20 to 40 pounds following operation. Postoperative weight loss has always been a problem of concern in the woman subjected to gastric resection. In the Billroth I group, one out of 6 women operated upon for duodenal ulcer developed postoperative weight loss; whereas one out of 3 women undergoing a Billroth II reconstruction showed loss of weight. It should be emphasized again that 3 patients undergoing radical resection for gastric ulcer with a Billroth I reconstruction showed no weight loss in the postoperative period. However, 3 patients subjected to radical resection for gastric ulcer in the Billroth II group show postoperative weight losses.

We have observed, as have others, that postoperative weight loss constitutes more of a problem in the patient who is underweight or below ideal weight prior to operation. In this type patient, a Billroth I reconstruction is preferred and is carried out in all cases where the duodenal ulcer can be safely removed and a normal cuff of duodenum mobilized for the anastomosis. Two-thirds of the weight losses in the present Billroth II group were represented by this type individual. In our experience the large, obese individual has presented no problem in regard to weight loss following operation. These patients are usually subjected to a Billroth II reconstruction for reasons previously stated.

Anemia was not a problem in either group of patients following operation. No doubt, the conservative resection employed in most cases was responsible for the infrequency of this complication.

Symptoms of the dumping syndrome were encountered more frequently in the Billroth II group and this observation is in accord with the reports of others. The symptoms were of extreme severity in 5 patients of this group and reoperation with conversion to a Billroth I was necessary in 2 instances as cited elsewhere. In one of these patients prior to reoperation, a challenge with an oral test meal consisting of 150 c.c. of 50 per cent glucose was productive of marked symptoms of weakness, palpitation, diarrhea, and sweating. An associated 34 per cent decrease in the circulating blood volume was noted. Following conversion to the Billroth I reconstruction, a similar challenge produced no appreciable drop in the circulating blood volume and only transient dizziness was experienced. The clinical improvement in both patients has been indeed striking following reoperation. The 3 remaining patients with severe dumping symptoms were women.

Dumping symptoms were generally of a milder nature in the Billroth I patients and in no instance did they constitute a troublesome postoperative problem. Durham[4] mentions the dumping syndrome present in 25 per cent of his Billroth I patients, but for the most part the symptoms were of a transitory

nature. He felt that he could predict with relative accuracy prior to operation which patients would complain of these symptoms by a thorough study of the patient's personality.

Patients undergoing a Billroth I reconstruction following antral resection and vagotomy for treatment of duodenal ulcer have not been followed for a sufficient time period in order to evaluate recurrence rates. At present, only one recurrence in the group operated upon for duodenal ulcer is encouraging. There is a definite possibility that an incomplete vagotomy may have accounted for this one recurrence. Walters[17] cites an increased incidence of recurrent ulceration after a Billroth I reconstruction, as compared to the Billroth II, but it must be emphasized that he did not include a vagotomy as part of the operation. In the present study, the absence of a suspected or proved recurrence in 180 patients undergoing vagotomy, antrectomy, and a Billroth II reconstruction for duodenal ulcer is of increasing interest. The one recurrence following a Billroth II reconstruction for gastric ulcer occurred in a 48-year-old man approximately 24 months after he underwent an estimated 60 per cent resection for a lesser curvature lesion. He was reoperated upon and approximately 15 per cent more of the stomach was removed with conversion of the Billroth II reconstruction to a Billroth I. He has done extremely well over a 2½ year follow-up. The patient has expressed repeatedly that he experiences less digestive complaints and is better satisfied with the Billroth I reconstruction than he was with the Billroth II prior to the development of symptoms suggesting a recurrent ulceration.

The over-all excellent and good postoperative results among the Billroth I and Billroth II groups are approximately equal, 92 and 90 per cent, respectively. However, there is a larger percentage of patients in the Billroth I group who obtained excellent results, as compared to the Billroth II group. Almost one-half of the patients obtaining fair and poor results among the Billroth II group were women. There were no patients in the Billroth I group who complained of gastrointestinal disturbances of such a nature that he or she could not pursue a useful occupation.

The Billroth I reconstruction, along with vagotomy and antral resection, has given slightly better over-all results to date in our experience in the surgical management of duodenal ulcer. The recurrence rate in this group, however, cannot be adequately evaluated for some years hence. As a result of this study, it appears that the Billroth I reconstruction at present is being employed in most instances where the duodenal ulcer can be removed safely and without difficulty. Particularly is the method advantageous in the individual who is underweight or below ideal weight prior to operation. Our experience bears out that every effort should be made whenever technical considerations permit to perform the Billroth I reconstruction when operating upon a woman either with gastric or duodenal ulcer. The Billroth I reconstruction, in addition, can usually be utilized in most men undergoing operation for benign gastric ulcer. Our experience with resection for gastric ulcer is indeed limited, but accumulated data show that recurrence rates following operation are strikingly low. The Billroth II reconstruction has proved to be the safest, as well as the preferred method,

when operating upon the large, posterior, penetrating duodenal ulcer which cannot be safely or completely removed. Also, this latter method is more suitable for the obese individual who presents certain technical problems in operative management.

SUMMARY

A clinical study of 2 groups of patients with benign gastroduodenal disease has been presented. One group was subjected to gastric resection with a Billroth I reconstruction, while another group underwent resection with a Billroth II reconstruction.

Vagotomy was employed in each patient in both groups presenting with a duodenal ulcer.

A comparison of hospital complications and follow-up results in both groups of patients have been cited and discussed.

Relative indications are presented for the selection of either a Billroth I or Billroth II reconstruction when operating upon the patient with a benign gastric or duodenal ulcer.

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SUBPHRENIC ABSCESS

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THE surgeon who practiced his profession in the preantibiotic era was much more aware and correspondingly more alert to the possibility of the development of a subphrenic abscess following an intra-abdominal catastrophe than are surgeons whose experience dates from this time. The same applies to localized collections of pus elsewhere in the abdomen, particularly in the pelvis. It has been my observation that interns and residents in our hospitals have rarely and sometimes have never seen a subphrenic abscess and, when such a complication does occur, they are very prone to conclude that the primary trouble is pulmonary rather than below the diaphragm. For this reason I believe it is important to discuss this problem from time to time, because a subphrenic abscess is always a very serious complication and, if not recognized fairly early and treated adequately, frequently results in a fatal outcome.

In 1933, before the Hawaii Territorial Medical Association, I discussed this subject and at that time quoted from Whipple[3] as follows: "In 1,000 cases of subphrenic abscess, 30 per cent were found secondary to lesions of the stomach or duodenum—usually perforated ulcer; 21 per cent followed a ruptured appendix and 16 per cent were secondary to infections in the biliary tract. The remainder occurred in association with lesions of the kidney, spleen, pancreas, lungs, etc." He found that when the condition was recognized early and adequately treated, the mortality rate was between 20 and 50 per cent and when not recognized was practically 100 per cent unless spontaneous rupture occurred.

In 1930, Ochsner and DeBakey[2] made an extensive study of the problem of subphrenic abscess and reported on 3,608 cases which included those they had encountered. The analysis showed that subphrenic abscess is primarily a complication of an intra-abdominal suppurative process, revealed by the fact that the primary lesion was in the abdomen in 84 per cent of the cases. Well over half were found to be the result of suppurative lesions of the appendix and perforative lesions of the stomach and duodenum. It was their conclusion that, rarely, the mechanism of spread of the infection to the subphrenic spaces occurred through vascular channels, most frequently through intraperitoneal or extraperitoneal direct invasion, or by way of the lymphatics. It was their belief at that time that approximately 70 per cent of suspected subphrenic abscesses cleared up spontaneously without proceeding to suppuration. No doubt, with present-day widespread use of antibiotics when an impending infection is suspected, many more such infections fail to reach the suppurative stage.

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Any individual, following an abdominal operation—particularly one where infection is present at the time—is a potential candidate for the development of a subphrenic abscess. Such an individual apparently may be making a satisfactory postoperative recovery for several days, perhaps weeks, before evidence of such a complication is observed. This is particularly so in the individual who has been under antibiotic therapy and who has not been under such circumstances these days. Following surgery for the various predisposing conditions mentioned, if the patient begins to complain of not feeling well and exhibits low-grade fever, usually associated with leukocytosis, and no apparent cause can be detected, the possibility of a beginning subphrenic abscess must always be considered. A careful examination of the individual may or may not suggest this possibility at this time. Tenderness beneath the right costal margin or posteriorly along the course of the twelfth rib or following percussion over the lower chest or right flank is a finding suggestive of this condition. If to these findings is added dullness to percussion over the right lower chest posteriorly with absent breath sounds, one's suspicions should certainly be aroused. Even in the absence of evidence of a very convincing nature, fluoroscopic and x-ray study should be made to see if the diaphragm moves normally with respiration, if it is higher than it should be, or if air is present in the subphrenic space. While the vast majority of such abscesses develop on the right side, the left is not immune and similar findings on the left indicate a subphrenic abscess in this area.

The most frequent complication of a subphrenic abscess is pleurisy frequently accompanied by a serous exudate. This, according to Ochsner and DeBakey, is indicative of a late diagnosis, although I believe in most people's experience this frequently occurs before the abscess is really diagnosed and drained. The exudate in the pleura may become purulent, producing an empyema when the diaphragm and base of the lung become united by adhesions. The abscess may perforate into a bronchus without infecting the pleural cavity, and the patient may cough up varying amounts of purulent exudate. If the original subphrenic infection is recognized early and treated properly, such complications do not occur. As Ochsner and DeBakey succinctly put it, evacuation of a subphrenic abscess by way of the bronchus is Nature's solicitous attempt to mitigate our lack of proficiency.

The literature dealing with subphrenic abscess for the most part includes all abscesses lying above the transverse colon. Abscesses lying subhepatically, usually around the region of the gall bladder and those in the lesser omental cavity and beneath the left lobe of the liver when localized to these areas usually give signs and symptoms that differ considerably from those lying in immediate contact with the undersurface of the diaphragm. Epigastric and subcostal tenderness is usually more marked and pain and tenderness posteriorly over the lower chest do not usually occur. Physical findings, such as dullness to percussion, absent breath sounds over the lower chest, and x-ray evidence of a high diaphragm with fixation, are not to be expected.

For an adequate description of the site of a subphrenic abscess and the best method of approach for its drainage, it is necessary to be familiar with

certain anatomic landmarks about the liver, particularly those spaces created by the reflections of the falciform and coronary ligaments as they course over the dome of the liver. The relationship of the pancreas to the lesser omental cavity and the possibility of an abscess of the pancreas usually as a sequel to an attack of acute pancreatitis rupturing into this cavity should be remembered. Two such occurrences took place in the series of cases being reported.

Another site of a subphrenic abscess unusual but well worth remembering is the extraperitoneal area over the top of the liver formed by the diverging leaves of the falciform ligament as they turn to the right and to the left to form the coronary ligaments. Many years ago an individual had his abdomen drained for a ruptured appendix while at sea. Several days later I removed the appendix and drained an abscess extending up along the lateral aspects of the ascending colon. He later developed a subphrenic abscess above the liver on the right which was drained. Several days after this, a right subhepatic abscess was drained. The patient died and autopsy revealed another unrecognized abscess in the extraperitoneal area described above. Had this abscess been recognized and drained, I have reason to believe that the patient would have recovered.

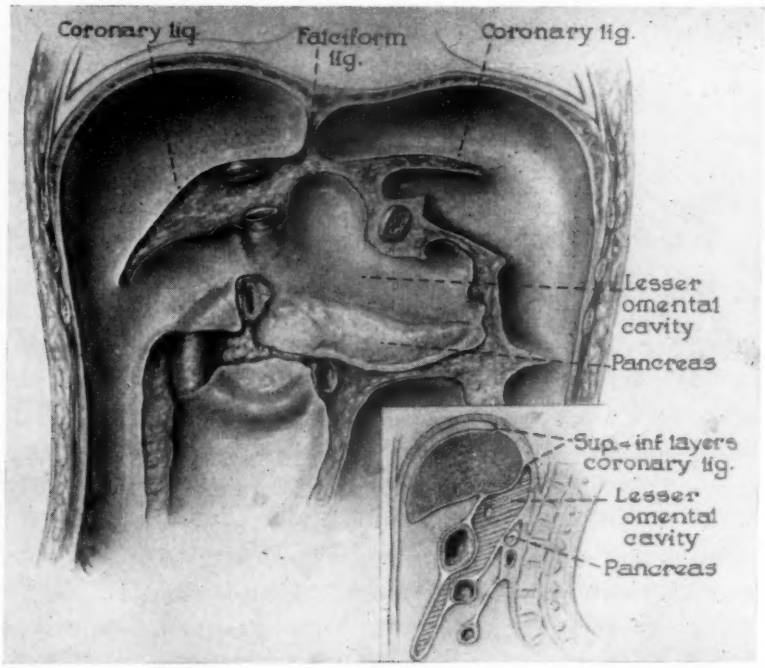

Fig. 1.—The anatomy in the subphrenic area one should be familiar with in dealing with subphrenic abscess.

The accompanying drawing (Fig. 1) illustrates the peritoneal reflections about the liver and other anatomic data important to remember when considering the subject of subphrenic abscess. Briefly, the falciform ligament extends from the umbilicus upward over the anterior superior surface of the liver and divides this organ into the right and left lobes. Posterior superiorly, the leaves of the falciform ligament separate and turn to the right and to the left to form the coronary ligaments; continuation of which forms the right and left triangular

or lateral ligaments of the liver. These reflections of the peritoneum have led to the generally accepted division of the spaces about the liver as follows: (A) intraperitoneal—right anterior subphrenic area proper, and posterior subhepatic area and left anterior subphrenic area proper posterior lesser omental cavity and (B) extraperitoneal—right and left.

Gerwig and Blades,[1] before the American Surgical Association in 1956, discussed the subphrenic abscess problem and emphasized the necessity for its re-evaluation due to the camouflaging effects of antibiotics. They found that, as long as bacterial suppression is present, the patient may appear to be in good physical condition, but escape from the influence of antibiotic drugs can be quite rapid and these patients may become desperately ill within a few hours and drastic measures may be necessary to save life.

Altemeier, in discussing this paper, further emphasized the masking effects of antibiotics, particularly their prophylactic use in increasing the difficulty of diagnosis of subphrenic abscesses. He advised discontinuing all antibiotics if general signs of infection are present without evidence of localization. This will permit localizing signs to develop.

TREATMENT OF SUBPHRENIC ABSCESS

In the preantibiotic era, it was demonstrated to be extremely important to drain subphrenic abscesses without contaminating the pleura or the peritoneal cavity. Those lying anteriorly can frequently be approached extraperitoneally by carefully mobilizing the parietal peritoneum from the undersurface of the diaphragm entering the abscess through adhesions which wall it off from the general peritoneal cavity. Those lying posteriorly can be drained extraperitoneally and extrapleurally by resecting the twelfth rib entering the area between the upper part of the kidney and the lower border of the liver opposite the spinous process of the first lumbar vertebra. With the present protection offered by antibiotics, the danger of peritonitis developing when this method of drainage cannot be accomplished is much less likely to occur. However, this should not encourage one to disregard the advantages of staying out of the general

TABLE I. INCITING FACTORS GIVING RISE TO SUBPHRENIC ABSCESSES

Appendectomy		12
Appendix ruptured	11	
Appendix not ruptured	1	
Resection of stomach		10
For carcinoma (1 with resection of transverse colon)	3	
For gastric ulcer (1 perforated)	3	
For duodenal ulcer	4	
Perforated gastric ulcer simply closed		1
Cholecystectomy		6
Ruptured gall bladder, abscess formation	2	
Empyema of gall bladder	1	
For stones	3	
Acute diverticulitis of colon		2
Abscess of liver, ascending cholangitis secondary to sphincterotomy for recurrent common duct stones		1
Abscess following acute pancreatitis		2
Perirenal infection		2
Cause unknown		5
	Total	41

peritoneal and pleural cavities. Most such subphrenic abscesses can be adequately drained by a subcostal approach. Whatever the method used, the objective is to gain free and dependent drainage. It is gratifying to note how quickly most intra-abdominal abscesses clear up after free drainage and proper use of antibiotics in comparison with the long period of suppuration and sloughing out of tissue so routinely encountered in earlier years.

A review of our experience with subphrenic abscess discloses that 41 cases have come to surgical drainage. The inciting factors giving rise to the subphrenic infection are tabulated in Table I. The following case reports illustrate some of the aspects of the problem previously discussed.

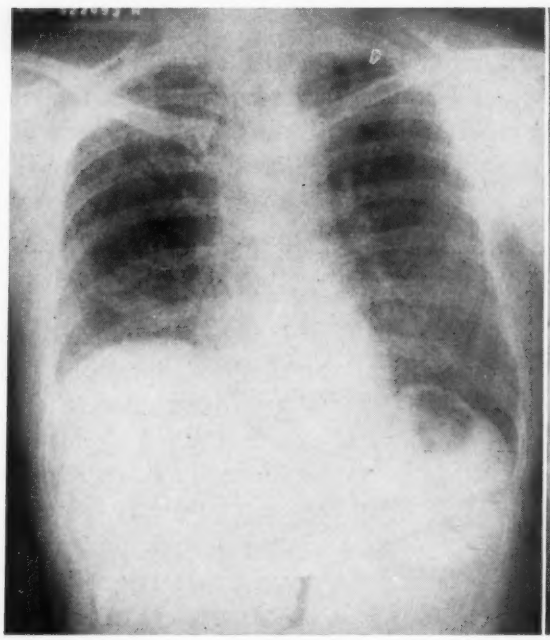

Fig. 2.

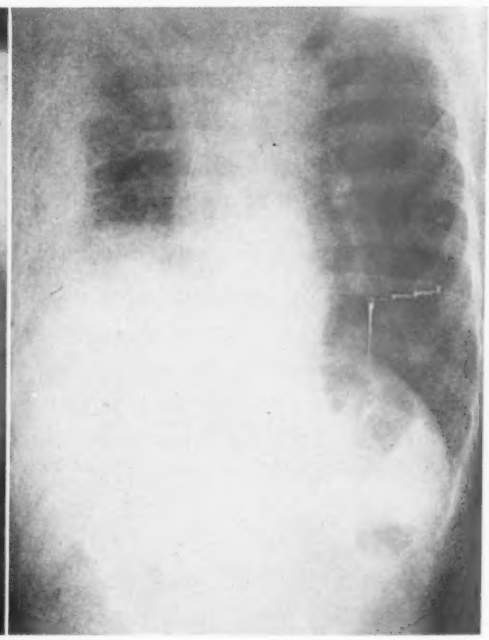

Fig. 3.

Fig. 2.—Case 1. High diaphragm on right side.
Fig. 3.—Case 1. High diaphragm on right with pleural effusion 3 weeks after x-ray shown in Fig. 3.

CASE REPORTS

CASE 1.—A Japanese man, aged 67, was seen for his present trouble on Nov. 14, 1957. He was complaining of discomfort in the right lower chest and pain in the right shoulder. Temperature was 101° F.; white blood count was 22,700 with 83 per cent polys. X-ray of his chest (Fig. 2) showed a high right diaphragm with absent breath sounds and dullness over the right lower chest posteriorly. He was referred into the hospital with a tentative diagnosis of a subphrenic abscess. He was started on penicillin, Aureomycin, and streptomycin. His temperature quickly fell to normal and his symptoms abated. He left the hospital in a few days' time feeling quite well.

This patient was next seen on Dec. 4, 1957, three weeks later, at which time he looked quite ill. He had no fever; the physical findings were as before. X-ray of the chest (Fig. 3) again showed a high diaphragm but with pleural thickening and free fluid. The white cell count was 16,500 with 90 per cent polys.

I had operated upon this patient on Oct. 31, 1950, and multiple stones were removed from the common and hepatic ducts. Ten years prior to this, his gall bladder had been

removed for stones. Again on Jan. 6, 1953, multiple stones were removed from the biliary tree and a transduodenal sphincterotomy of the ampulla of Vater was carried out. On Dec. 5, 1957, a gastrointestinal study showed air in the biliary tree (Fig. 4) and barium given orally filled a much dilated common duct (Fig. 5).

At operation on Dec. 7, 1957, a few stones and debris again were removed from the dilated common duct which was drained. A large subphrenic abscess over the dome of the liver was found which appeared to arise from an abscess of the liver and which was thought to be secondary in all probability to regurgitation of food up the common duct. The patient subsequently developed an empyema necessitating drainage.

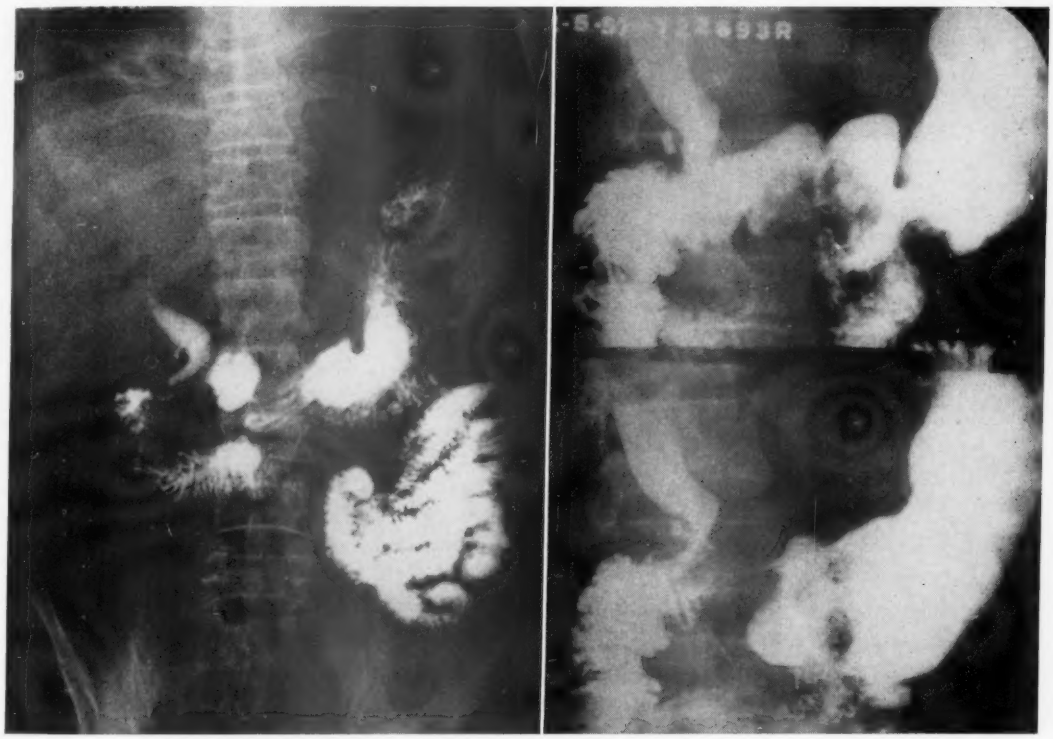

Fig. 4. Fig. 5.

Fig. 4.—Case 1. Air in biliary tree following sphincterotomy of ampulla of Vater.
Fig. 5.—Case 1. Dilated common duct filled with barium.

CASE 2.—A Japanese woman, aged 48, had a high radical gastric resection for carcinoma of the stomach on July 7, 1953. Nine days later, because of fever, leukocytosis, and an x-ray showing a high diaphragm on the left (Fig. 6), the left subphrenic space was explored and a large abscess was found and drained. The patient recovered satisfactorily.

CASE 3.—A Japanese man, aged 76, was first seen on June 29, 1953, complaining of right upper quadrant pain associated with a temperature of 102° F. and white blood count of 15,000. He had been ill for about 10 days. There was dullness to percussion over the right lower chest. There was very little tenderness to palpation or percussion over the right upper abdomen and lower chest. X-ray (Fig. 7) showed cloudiness in the right lower thoracic cavity and a high diaphragm. At operation through a right subcostal incision, a large amount of pus was evacuated from the area between the diaphragm and the liver and subhepatically around the region of the gall bladder. The infection had evidently arisen from perforation of the gall bladder. The patient made an uneventful recovery following adequate drainage and the use of antibiotics.

CASE 4.—A Japanese man, aged 57, on July 2, 1956, had a contracted gall bladder containing stones removed and a stone removed from the common duct. The common duct was drained. The patient was returned to surgery a few hours later because of hemorrhage from a branch of the cystic artery. Eleven days later a large subphrenic abscess on the

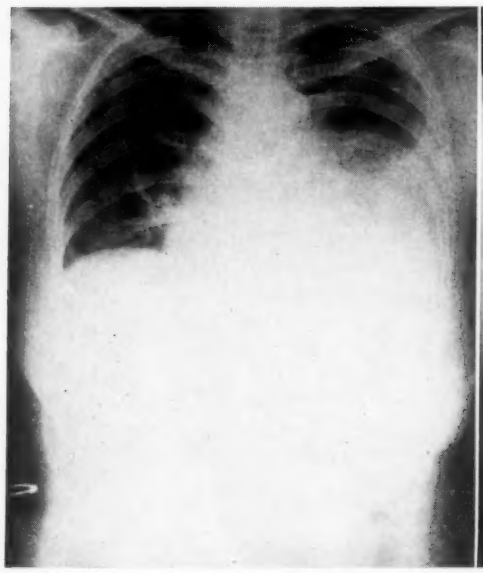

Fig. 6.

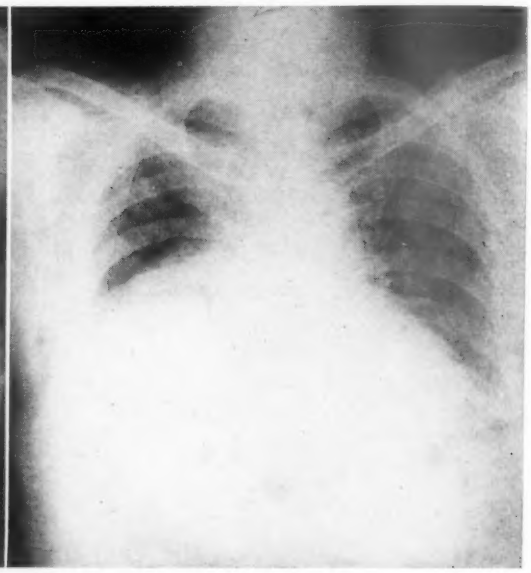

Fig. 7.

Fig. 6.—Case 2. High diaphragm on left due to subphrenic abscess following high gastric resection.

Fig. 7.—Case 3. High diaphragm and cloudiness in right lower pleural cavity secondary to subphrenic abscess secondary to perforation of acute cholecystitis.

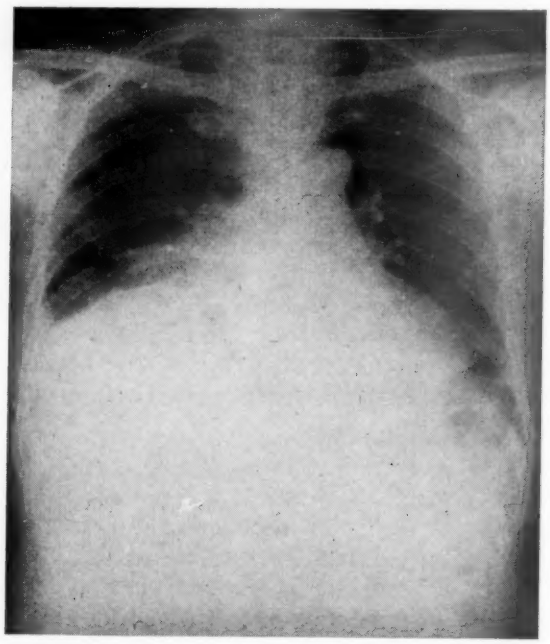

Fig. 8.—Case 4. High diaphragm on right with cloudiness of pleural space secondary to cholecystectomy followed by hemorrhage.

right was drained. For several days previous to this, the patient had had temperature as high as 102° F., white cell count up to 32,000, and some tenderness along the right subcostal area. There was dullness over the right lower chest and x-ray (Fig. 8) showed elevation of the right diaphragm and cloudiness in the base of the right lung. The patient made an uneventful recovery.

CASE 5.—The case of a Caucasian man, aged 43, was diagnosed as having gallstones with a nonfunctioning gall bladder by history and x-ray findings in August, 1942. He was advised to have a cholecystectomy but he failed to have this done.

On Jan. 17, 1944, he developed acute pain in the gall bladder region associated with fever, leukocytosis, and tenderness over the gall bladder region. Forty-eight hours later an acutely inflamed gall bladder containing stones was removed. There were numerous areas of fat necrosis in the omentum and in the gall-bladder area indicative of acute pancreatitis. Eight days later, because of rising fever, high white blood cell count, and tenderness along the left costal margin, the abdomen was explored. A large amount of purulent fluid was drained from the lesser omental cavity. The patient recovered uneventfully.

COMMENT

I would like to emphasize that, while subphrenic abscess occurs less frequently than before the use of antibiotics, it is still a complication of surgery to be reckoned with. Since subphrenic abscess usually occurs in individuals debilitated from the original illness which has usually been of a serious nature, the morbidity and mortality continue to be of serious consequence. Early recognition and adequate drainage of the abscess cavity is of the utmost importance if a satisfactory recovery is to be expected. The masking effects of antibiotics tend to obscure symptoms and signs previously relied upon to call one's attention to such a complication. Being aware and alert to the possibility of a subphrenic abscess developing following the more commonly encountered conditions in which this complication arises, such as a ruptured appendix, duodenal or gastric ulcer, or acute infection of the gall bladder, is a big factor in the early recognition. A sufficient number of such abscesses occur following gastric resection where the viscus has not ruptured and after cholecystectomy without infection to make one suspicious of this possibility when the patient fails to recover in an expected manner. The individual failing to recuperate satisfactorily following upper abdominal surgery who has a fever of varying heights associated with leukocytosis and tenderness along the subcostal margin has a subphrenic abscess until this possibility is disproved. He may well have such a complication without as many suggestive findings. Under such circumstances, the finding of dullness in the lower thoracic cage with râles, bronchial breathing, or absent breath sounds is certainly more indicative of trouble below the diaphragm than it is of a primary lesion in the lung. If, along with these findings, x-ray study reveals a high fixed diaphragm, one may be assured that he is dealing with a subphrenic abscess and surgical intervention is indicated.

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DIAPHRAGMATIC DEFICIENCY IN THE RETROCOSTOXIPHOID AREA

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CLINICAL FEATURES

HERNIA through defects in the retrocostoxiphoid area is becoming more frequently detected. One chest unit has recently reported 33 patients having been seen with this condition over a short period of time.[1]

Most patients will be asymptomatic. Some will have respiratory symptoms. Despite the protrusion of colon, omentum, and stomach into the opening, few patients will have gastrointestinal symptoms. The bowel is rarely obstructed.

The roentgenograms show a soft tissue density at either anterior cardiophrenic angle. The entity may be indistinguishable roentgenologically from affections of the lung, particularly those of the middle lobe, empyema, pericardial hernia, pleuropericardial cyst, hydatid cyst, localized eventration, and other conditions.

Omentum is usually present and casts a dense shadow (Figs. 1 and 2). If bowel filled with gas is in attendance, the hernia has a honeycombed appearance and is more radiolucent than the adjacent lung field (Fig. 3).

Fluoroscopic observations of the diaphragm yield little information not gained in other roentgenologic examinations. Localized eventration and hernia are difficult to differentiate by this method, since both give the false appearance of having the same diaphragmatic motion.

Of little help ordinarily, the upper gastrointestinal study with barium may depict gastric distortion and elevation. The stomach is pulled upward by its omental and colonic attachments.

Barium enema is more likely to demonstrate the hernia. The barium-filled colon continued within the chest assumes the contour of an "O" or inverted "U" (Figs. 4 and 5). Despite this study, a high diaphragm may simulate an actual hernia (Figs. 6 and 7).

Pneumoperitoneum is a diagnostic aid. Separation of the herniated structures from the lung by this maneuver permits their radiologic characteristics to be brought out more clearly (Figs. 8, 9 and 10). If, as sometimes happens, the organs are adhered to the hernial lining, no air is interposed between them and the lung, and the procedure is of no diagnostic value.

The treatment is surgical. The commonly recommended approach is through the abdomen. Recently interest has been revived in the transthoracic route. No great difficulty was experienced in the Charity Hospital series with either

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approach. Either can be converted to a thoracoabdominal incision with ease. The sac is usually excised. The muscle edges are freshened and sutured to the posterior surface of the xiphisternum and costal arch. The round ligament may

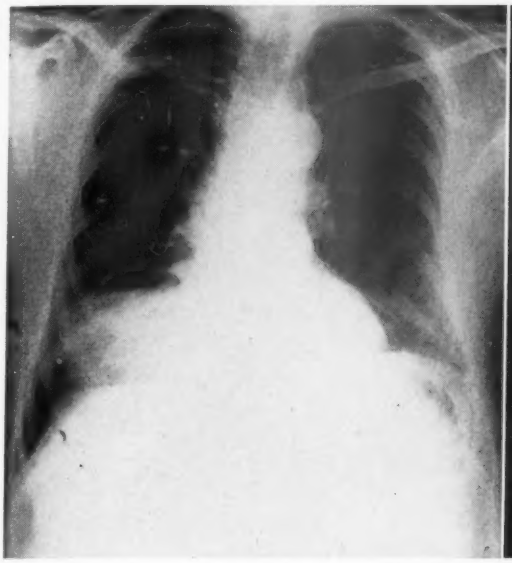

Fig. 1.

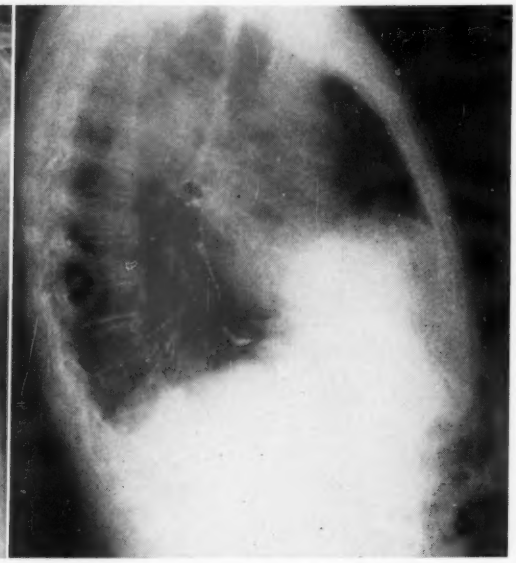

Fig. 2.

Fig. 3.

Figs. 1, 2, and 3.—Herniation of abdominal contents into chest through deficiency in the retrocostoxiphoid area. The first two roentgenograms show a soft tissue density in the right anterior cardiophrenic angle. In Fig. 3 bowel contained within the chest gives a honeycombed appearance to the hernia.

be used to reinforce the repair. Fascia lata and other materials may be used to cover a large defect. Even with a difficult closure, phrenic crush would seem to have little merit as an adjunctive procedure.

CASE REPORTS

This study is based upon a survey of diaphragmatic hernia at Charity Hospital of Louisiana from 1937 to the present. Of 81 patients upon whom operation was performed for diaphragmatic hernia, 5 had defects in the retrocostoxiphoid portion of the diaphragm repaired.

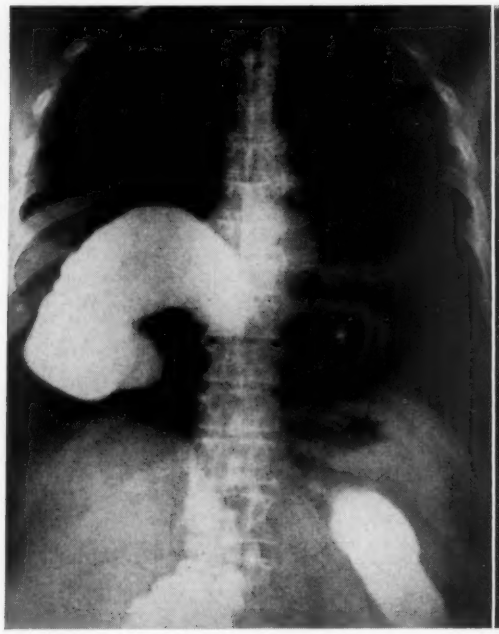

Fig. 4.

Fig. 5.

Figs. 4 and 5.—Barium enema is more likely to demonstrate the hernia, and in these figures the colon can be seen to project into the thoracic cavity. The diagnosis was confirmed at operation.

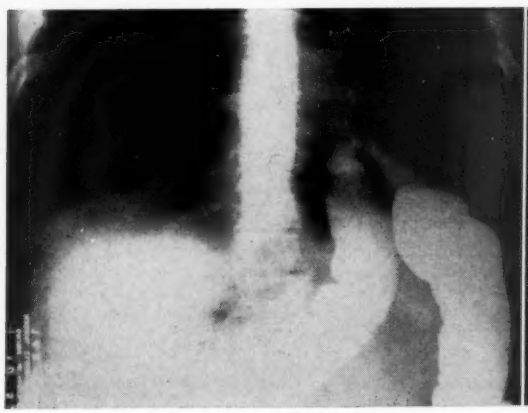

Fig. 6.

Fig. 7.

Figs. 6 and 7.—Barium-filled colon *apparently* projects into the chest through anterior deficiency in the diaphragm. No hernia was encountered at operation. The diagnosis was partial eventration of the diaphragm.

CASE 1.—F. L., a 54-year-old white man, was admitted to the hospital on May 11, 1955, and discharged on July 2, 1955. He had had pneumonia and pleurisy in 1935 and was now in the hospital for repair of an inguinal hernia. A preoperative roentgenogram of the chest showed a dense opacity in the anterior cardiophrenic angle on the right. The right leaf of

the diaphragm moved paradoxically on respiration. The barium-filled midtransverse colon was visible in the right cardiophrenic angle of the chest, and the afferent and efferent limbs of the bowel were constricted in the retrocostoxiphoid area. Excess mucus was found in the tracheobronchial tree during bronchoscopy. On June 18, 1955, under endotracheal anesthesia,

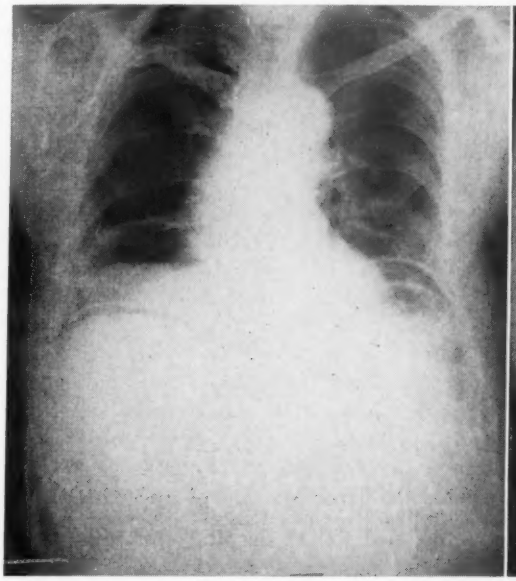

Fig. 8.

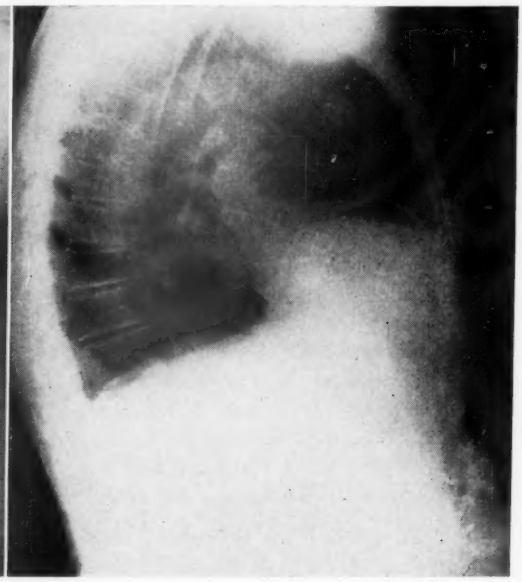

Fig. 9.

Fig. 10.

Figs. 8, 9, and 10.—Pneumoperitoneum permits separation of the herniated abdominal structures from the lung. By this maneuver the radiologic characteristics are brought out more clearly.

the abdomen was opened through a right paramedian incision. The diaphragmatic defect was retroxiphoid, in the midline, and contained midtransverse colon, omentum, and part of the stomach. The sac was excised and the muscle was sutured to the xiphoid, sternum, and costal cartilages. Postoperatively he had a collapse of the right lung, and after 1,150 c.c. of air was removed from the chest the lung expanded.

CASE 2.—C. J., a 43-year-old Negro woman, was admitted to the hospital on June 13, 1948, and discharged on July 10, 1948. She was complaining of pain in the chest. She had had subphrenic abscess previously. The right leaf of the diaphragm was elevated and the opacity extended to the third rib. With barium in the intestinal tract, the colon and small bowel could be traced into the chest through a defect in the anterior diaphragm. On June 28, 1948, the abdomen was explored through a right rectus incision and a 6 cm. opening in the right parasternal area was found. The sac was excised and the diaphragmatic defect closed.

CASE 3.—L. S., a 69-year-old white man, was admitted to the hospital on Sept. 9, 1953, and discharged on Sept. 24, 1953. He had begun with an acute episode of influenza in February, 1953, and continued with a wheezing cough which was productive of small amounts of phlegm. An oval density in the right anterior subdiaphragmatic portion of the thorax was seen on roentgenograms. A barium enema was thought to be normal. A bronchogram was performed; the bronchi of the right middle lobe did not fill well. The bronchoscopy was normal. Bronchial washings were reported to contain cells consistent with malignancy. On fluoroscopic examination, the liver and the density moved synchronously with diaphragmatic excursion. Needle aspiration of the mass yielded tissue from the liver. Although the lung was apparently well outlined away from the mass, an intrapulmonary lesion was the interpretation of the roentgenograms taken after pneumoperitoneum. On Sept. 11, 1953, with the patient under endotracheal anesthesia, the chest was opened through the bed of the right sixth rib and a hernia through the foramen of Morgagni was found. The sac contained omentum. After the sac was excised the defect was closed without difficulty.

CASE 4.—S. F., a 5-year-old white girl, was admitted to the hospital on May 1, 1951, and discharged on May 23, 1951. She had had a coarctation of the aorta resected Aug. 8, 1950. Since then she had failed to gain weight. A 4 cm. density was present, confluent with the right cardiac border and in the anterior costophrenic angle. The tentative diagnosis was a pericardiac celomic cyst. On May 15, 1951, with the patient under endotracheal anesthesia, the chest was explored through the right sixth intercostal space. A foramen of Morgagni hernia was identified, the sac excised, and the defect closed without difficulty.

CASE 5.—S. S., a 2-year-old white boy, was admitted to the hospital on March 10, 1952, and died on April 8, 1952. He had had fever since birth. Three days prior to admission he developed severe vomiting and diarrhea, and when examined he was acutely ill. A bowel shadow was present in the chest, consistent with foramen of Morgagni hernia. The condition of the patient became even more critical in the hospital, and operation was undertaken on April 8, 1952. With the patient under open drip anesthesia, the abdomen was opened through an upper midline incision. The hernia sac was excised and the edges sutured to the costal margin. At this point in the procedure cardiac arrest occurred, and resuscitation was unsuccessful.

HISTORICAL BACKGROUND

Wrote Morgagni in 1761 concerning defects in the anterior portion of the diaphragm[5]:

> "There certainly are places in the diaphragm, through which, upon drawing asunder of the fleshy fibers, and upon the giving way of the membranes, the stomach, or some part of the intestinal tube, or any other viscus, may pass over from the belly into the thorax . . . anteriorly, between the fibers there generally is an interval through which something . . . may happen . . . in a husbandman . . . part of the intestine carried up, through the . . . anterior part of the diaphragm . . . neither this intestine, nor the foramen, the diameter of which was two thumbs breadth, and through which this part went out and came in, showed any sign of foregoing violence or disorder, and that the man died in decrepit age, from a manifest injury within the skull; I chose rather to suppose that it had been thus from the original formation . . ."

A lucid account of herniation through a diaphragmatic defect in the retrocostoxiphoid area, and one of the first to appear in the English literature, is that by Sir Astley Cooper, who, in 1798, set forth the pathologic picture thusly[2]:

> ". . . in the month of October, 1796 . . . a man aged fifty years, who had died from excessive vomiting after the use of an emetic, and in whom the viscera of the cavity of the abdomen were found disposed in an unusual manner . . . of the omentum only a small part could be seen; and the right extremity of the stomach, as well as the arch of the colon, had entirely disappeared. On inspecting the thorax a sac considerably larger than a tennis ball was found in its right cavity, which contained the right extremity of the stomach and beginning of the duodenum, a part of omentum, and the arch of the colon which was disposed in several convolutions. The sac was formed by the united membranes of the pleura and peritoneum, and its orifice was placed at a small distance from the right side of the ensiform cartilage, where there appeared a deficiency of fibers in the layer muscles of the diaphragm corresponding to the size of the sac. The parts which formed this hernia exhibited no marks of inflammation, were free from adhesions, and could be returned without difficulty into the cavity of the abdomen."

In the French literature the term "fente de Larrey" or space of Larrey is used to designate the foramen of Morgagni, especially in relation to diaphragmatic hernia. Larrey did not describe a hernia occurring through the diaphragm but did devise a surgical approach to the pericardium through the space which bears his name. Later French writers applied his name to the hernia which is found in this area. In Malgaigne's descriptive anatomy of the diaphragm, an allusion is made to the space behind the xiphoid, a triangular space with the sternum forming an anterior base.[4] Malgaigne goes on to say that at this point the cellular tissue meets with that of the abdomen and that this is the route Larrey proposed to follow to reach the pericardium.

Recently Thevenet[6] has traced the derivation of the term applied to the hernia to the same account in which Larrey discusses the anatomy of this region in relation to pericardiotomy. In the original description of the space Larrey[3] states:

> ". . . there exists constantly, especially on the sloping part (of the diaphragm), toward the xiphoid cartilage and on the side of the mediastinum . . . a cellular interval between the xiphoid cartilage and the extremities of the seventh and eighth ribs . . . lamellar tissue which is continued with that which is called the false lamina of the peritoneum . . . internal mammary artery passes a little more to the outside . . ."

This brief excursion into some of its historical precedents indicates that Morgagni antedated the other writers in describing this type of hernia. The name of Morgagni, commonly used in association with the hernia in the English literature, is more properly applied to the condition than that of Larrey.

ANATOMY

The muscle in its contribution to the musculotendinous diaphragm is peripherally distributed with 3 origins: sternal, costal, and lumbar. The sternal part arises by 2 fleshy slips from the posterior xiphoid. The costal part takes origin from the inner surface of the costal cartilage and adjacent lower 6 ribs on either side, interdigitating with the transversus abdominis.

The tendinous portion is centrally placed, surrounded by muscle. The tendon lies closer to the front than to the back of the thorax and is partially blended with the pericardium. The shape of the tendon is comparable to that of a 3-leaf clover. The right leaflet is the largest. The middle, directed toward the xiphoid process, is the next in size, and the left is the smallest. The sternal portion is the weakest, consisting of a few slender fasciculi arising from the posterior surface of the xiphoid process.

The diaphragm is pierced by a series of apertures. On either side behind the sternum a deficiency of muscle fibers is found between their sternal and costal attachments. These spaces transmit lymphatics from the liver and abdominal wall and the superior epigastric branch of the internal mammary artery. Pleura and peritoneum line the spaces. The apertures are the "foramina of Morgagni" or "Larrey's spaces."

When a hernia occurs in this region, the eponymic designation is that of Morgagni or Larrey. It is a direct hernia. With rare exceptions, a sac is present. The hernia usually protrudes to the right, occasionally to both sides, and rarely to the left. Retrosternal and parasternal types could not be distinguished in the Charity Hospital series.

In 83 cases of this type of hernia reviewed in the literature and at Charity Hospital, omentum and colon were contained in the sac in 47, omentum, colon, and stomach in 19, omentum in 10, colon and small bowel in 3, stomach in 2, colon and liver in 1, and small bowel in 1.

EMBRYOLOGY

The anterior, central, and lateral portions of the diaphragm have their origin in the transverse septum. The posterolateral component results from a joining of the pleuroperitoneal membranes, the dorsal mesentery, and the wolffian body. The posterior and central portions embracing the esophageal aperture are derivatives of the dorsal mesentery. Since the anterior portion of the diaphragm is derived solely from the transverse septum, it is not likely that faulty diaphragmatic development is responsible for the deficiency in the retrocostoxiphoid region.

Since the transversus abdominis and the diaphragmatic musculature interdigitate, the former's development may be implicated as a causative factor in the type of hernia under discussion. The transversus muscle, derived from primitive segments, traces origin to the somatopleure. The myotomes are divided into anterior and posterior compartments and the anterior is the last to receive its muscles.

Another etiologic factor may be retarded fusion of the anterior ribs, costal cartilage, and sternum. The sternum arises independently of the ribs.

During the fifth week the right and left mesenchymal bars of the sternum are formed and gradually fuse in the midline. Sternal separation allows accommodation of the yolk sac and afterward the liver and heart. In the tenth week the intestines return from the cord to the abdomen. The chest wall expands before the growing lungs and the mesial ventral line closes.

The condensation of the costal mesenchyme as a separate vertebral element occurs in the fifth week. The costal extension ventralward corresponds with pulmonary growth and expansion. At the end of the seventh week the ribs have effected a junction with the sternal bars.

That this hernia almost invariably has a sac negates the concept that the hernia is a persistence of the ventral portion of the pleuroperitoneal canal and that it is comparable to the sacless lumbocostal hernia through the foramen of Bochdalek.

Rather it would appear from recently reported observations that deformities exist principally in the xiphisternum and costal cartilages as a result of developmental retardation, and the failure of fusion of the septum transversum to the anterior chest wall is secondary to this phenomenon. Enlargement of a normal anatomic aperture through changes in the pleuroperitoneal pressures must also be considered in causation of the hernia.

SUMMARY

This study is based upon a survey of diaphragmatic hernia at Charity Hospital of Louisiana. Of 81 patients upon whom operation was performed for diaphragmatic hernia, 5 had defects in the retrocostoxiphoid portion of the diaphragm repaired.

This herniation occurs through the foramen of Morgagni or its immediate neighborhood and projects usually into the right side of the thorax.

These hernias may or may not be associated with clinical disturbances which may be digestive, respiratory, or both. The colon and omentum are frequent occupants of the sac. Roentgenologically the hernia is revealed by an opaque, radiolucent, or mixed shadow in the right anterior cardiophrenic angle of the chest. The roentgenologic differentiation is enhanced by barium studies of the gastrointestinal tract. Pneumoperitoneum yields further diagnostic information.

Repair of the hernia can probably be accomplished with equal facility through the chest or abdomen. The abdominal edges of the defect are sutured to the back surface of the xiphisternum and costal arch.

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SERUM DESOXYRIBONUCLEASE ACTIVITY AND PANCREATIC DAMAGE

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RECENT analyses of the incidence of hyperamylasemia have indicated that this condition occurs with diseases other than pancreatitis.[4, 8] Further, a number of commonly employed drugs may induce significant increases in the amylytic activity of serum.[22] We have completed statistical study of over 1,800 amylase determinations at this center which show that 20 per cent of the elevations in serum amylase levels are associated with disease other than pancreatitis.[1]

In view of the lack of diagnostic specificity in this laboratory determination, an investigation was made, in experimental animals, of alterations in the circulating levels of desoxyribonuclease (DNA) activity which was recently reported by Kowlessar and McEvoy[15] to be elevated during the breakdown of pancreatic tissue.

MATERIALS AND METHODS

Mongrel dogs weighing between 9 and 13 kilograms served as experimental animals. Seven groups, each consisting of 3 successfully prepared dogs were utilized for study. In all animals in which it was necessary to produce pancreatitis by surgical means, the abdomen was entered through a right rectus muscle-splitting incision and closed in the conventional manner. Intravenous Nembutal (30 to 35 mg. per kilogram of body weight) was used for anesthesia. The following methods which were employed in an effort to produce experimental pancreatitis were chosen to simulate the most common etiologic hypothesis of acute hemorrhagic pancreatitis.

Pancreatic Peritoneal Fistula.—The point where the main pancreatic duct enters the duodenum was isolated in 3 dogs. An oval-shaped full-thickness section of duodenum (1 by 1.5 cm.) surrounding the junction of the duct was removed; this allowed the main pancreatic duct to dangle and drain freely into the peritoneal cavity (Fig. 1). Coffey[5] found that without the duodenal mucosa no peritonitis resulted. He reasoned that the mucosa was necessary to activate trypsinogen, which in turn caused peritonitis. The duodenal defect was closed in 2 layers.

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Ligation of Both Pancreatic Ducts.—The main and accessory pancreatic ducts in each of 3 animals were isolated as they entered the duodenum and doubly ligated at this point with cotton. No injury to the gland resulted immediately from this procedure.

Intraparenchymal Injection of Trypsin.—Approximately 3 mg. of aqueous crystalline trypsin freshly dissolved in 3 ml. of isotonic saline was injected through a No. 26 gauge needle into the parenchyma of the pancreas of 3 dogs. Multiple sites were used so that trypsin was equally distributed over the entire gland. Each gland at the end of this injection seemed to be twice its normal size and diffusely edematous.

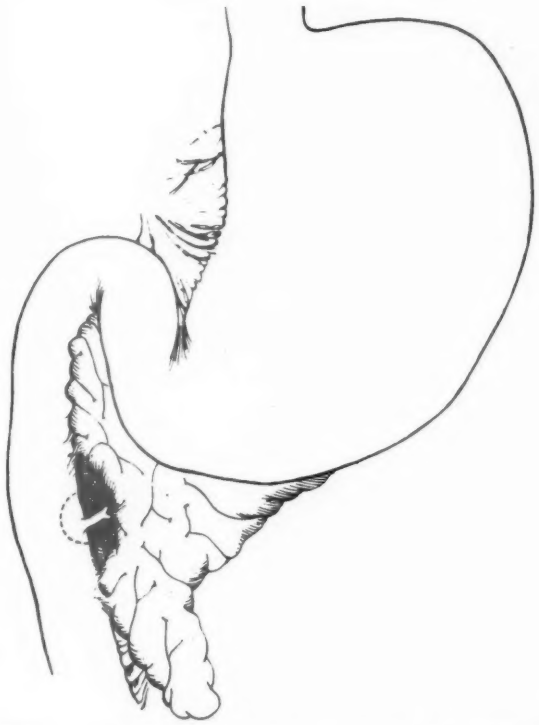

Fig. 1.—The method devised by Coffey[5] to produce a pancreatic peritoneal fistula utilizing a small amount of duodenal tissue to activate the released pancreatic enzymes.

Intraperitoneal Injection of Ethionine.—Approximately 25 mg. per milliliter of this amino acid was dissolved in water and the appropriate amount of fluid was injected intraperitoneally through a No. 18 gauge needle into each of 3 animals. A dosage of 100 mg. per kilogram of body weight was provided.[6] The animals received injections daily for 9 days without the aid of anesthesia.

Intraluminal Injection of Bile and Ligation of the Duct.—The major pancreatic duct was isolated and ligated in 3 dogs. About 5 ml. of preprandial bile was aspirated from the gall bladder of each dog and injected through a No. 22 gauge needle into the lumen of the main duct.[13] Shortly after injection, the whitish-pink gland was noted to have a green appearance and the minute blood vessels on the surface of the gland became dilated.[13]

Intraluminal Injection of Bile and Trypsin and Ligation of the Duct.—The major pancreatic duct was ligated in each of 3 dogs. Kheedroo[14] produced acute hemorrhagic pancreatitis by injecting 20 mg. of trypsin into the main pancreatic duct prior to ligation. Our experience showed that 20 mg. of trypsin produced pancreatitis of too fulminant a form for our purposes. Subsequently 4 ml. of an autospirate of preprandial bile was mixed with 1 ml. of a trypsin solution (5 mg. of crystalline trypsin freshly dissolved in 1 ml. of normal saline) and injected into the main pancreatic duct through a No. 22 gauge needle. The duct was doubly ligated with cotton in each of the 3 dogs.

Schwartzman Phenomenon[17].—About 5 ml. of a 1:2 dilution of meningococcic toxin obtained from the agar washings of cultures of strain 44-B* was injected into the main pancreatic duct of each dog through a No. 22 gauge needle. The duct was doubly ligated with cotton. Twenty four hours later a challenging dose of 5 ml. of a 1:10 dilution of this material was injected intravenously.

Blood Sampling Procedure.—After recovery, the dogs were allowed the usual chopped meat and biscuit diet which they had had prior to the experimental procedure. Blood (5 ml.) was drawn from the foreleg of each dog daily until death or for 7 to 9 days. The blood was allowed to clot. The supernatant serum was removed and frozen until a satisfactory number of specimens were collected to permit several determinations at one time.

The amylytic activity was assayed by a minor modification of the latest procedure of Smith and Roe.[19] The activity of 0.1 ml. of serum diluted 1:9 with buffer was expressed in terms of the number of micrograms of soluble starch depolymerized per milliliter in 30 minutes at 37° C. These units were termed S_d, or μg of substrate depolymerized, and were chosen for consistancy with the DNA units to be described. Twelve normal dogs had a mean activity of 12 ± 6 S_d, with a range of 2 to 24 units.

DNA activity was determined by a modification of the ribonuclease method of Houck[10] in which 0.5 ml. of a solution containing 600 μg of DNA dissolved in 0.05 M Veronal buffer (pH 7.2) was incubated with an equal volume of serum diluted 1:10 with 0.04 M magnesium chloride for 30 minutes at 37° C. The enzyme activity was halted by the addition of 5.0 ml. of 0.10 M acetate buffer (pH 3.7) containing 0.3 mg. per milliliter of serum albumin and 1 mg. per milliliter of Knox gelatin. After the addition of this reagent, the mixture was allowed to stand for 5 minutes at 37° C., during which time the acidified serum albumin formed a stable turbid colloid with the polymerized DNA remaining after enzyme action.

The absorbence of the turbidity so produced[10] was determined at 450 mμ in a Bausch and Lomb Spectronic "20". The optical density measured was compared to the optical density produced by various amounts of polymerized DNA and translated into micrograms of intact DNA remaining after

*The 44-B strain of meningococcus was prepared according to the method of Thomas and Good.[21]

30 minutes incubation. The difference between this value and the initial 600 μg per milliliter used was the number of micrograms of substrate depolymerized by 0.05 ml. of canine serum in 30 minutes of 37° C. These units were also expressed as S_d. The nature of these units has been discussed elsewhere.[11]

The mean DNA activity of 12 normal dogs was 90 ± 15 S_d, ranging from 62 to 118 units. Any values in excess of the mean DNA or amylase activity plus two times the standard deviation were considered statistically significant elevations.

A general description of the pathology of each gland determined from hematoxylin- and eosin-stained sections collected and prepared after the conclusion of each experiment is presented in Table I.

TABLE I. THE PATHOLOGICAL FINDINGS AFTER PANCREATIC DAMAGE

PROCEDURE	FINDINGS	HEMORRHAGE	NECROSIS	EDEMA	FIBROSIS
Fistula	Peritonitis				
Ligation	Fibrosis	0	0	+++	0
Trypsin	Mottling	+	+	++	+++
Ethionine	Hemorrhage	+	0	++	+
Bile, ligation	Hemorrhage and fibrosis	++++	++++	++	+++
Bile, ligation, trypsin	Fibrosis	++++	+++	++	+++
Schwartzman	Normal	+++	+++	+++	0

RESULTS

Pancreatic Peritoneal Fistula.—In the 3 preparations that were studied, no rise was observed in the serum level of DNA while a significant elevation in the serum amylase was found in each animal (Fig. 2). Gross pathologic examination of each pancreas was normal (Table I). A marked degree of hemorrhagic peritonitis with serosanguineous peritoneal fluid was seen in 2 dogs while all had fat necrosis in the omentum to a greater or lesser degree.

Ligation of Both Pancreatic Ducts.—Serum DNA activity was not increased in any of the 3 animals which were studied, while the serum amylase levels were profoundly elevated (Fig. 3). Each pancreas was small, fibrotic, and finely nodular. Microscopically there was an overwhelming accumulation of intraductal and acinar protein as well as interlobular hemorrhage and organization. Evidence of acinar necrosis and fibrosis was not noted, however (Table I).

Intraparenchymal Injection of Trypsin.—Fig. 4 shows a substantial rise in serum DNA activity in all 3 dogs which reached its peak on the eighth day. The serum amylase was consistently normal in all dogs. Grossly each pancreas at autopsy showed a pink mottling throughout, which was interpreted as evidence of microscopic hemorrhage. Some focal hemorrhage was seen on histopathologic examination but the notable pathologic change in all specimens was cellular edema (Table I).

Intraperitoneal Injection of Ethionine.—A slight elevation in the serum levels of DNA activity was seen in all 3 dogs on the first 3 postoperative days

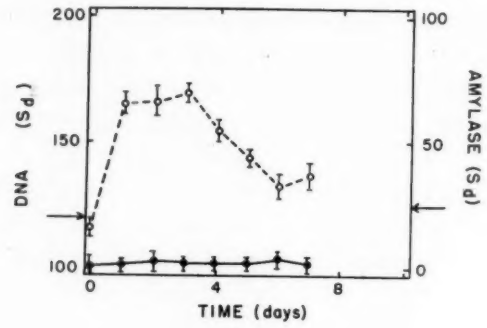

Fig. 2.

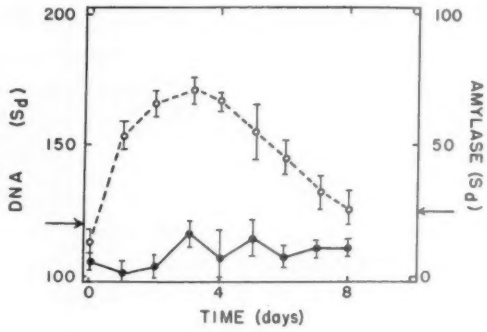

Fig. 3.

Fig. 2.—The effects of a pancreatic peritoneal fistula upon the mean DNA (●) and amylase (O) activity in the sera of 3 dogs. Vertical lines through each point represent the standard deviation, while the statistical upper limit of normal for each enzyme is indicated by arrows.

Fig. 3.—The effects of ligating both pancreatic ducts upon the mean DNA (●) and amylase (O) activity in the sera of 3 dogs. Vertical lines through each point represent the standard deviation, while the statistical upper limit of normal for each enzyme is indicated by arrows.

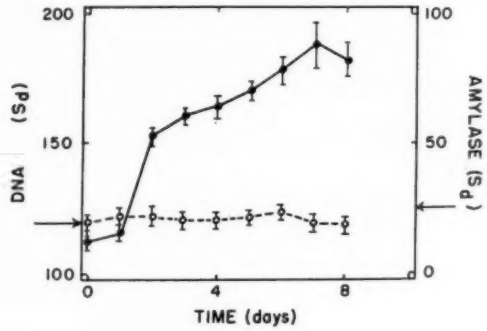

Fig. 4.

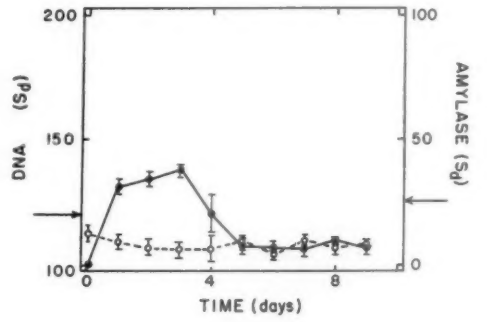

Fig. 5.

Fig. 4.—The effects of an intraparenchymal injection of trypsin upon the mean DNA (●) and amylase (O) activity in the sera of 3 dogs. Vertical lines through each point represent the standard deviation, while the statistical upper limit of normal for each enzyme is indicated by arrows.

Fig. 5.—The effects of repeated intraperitoneal injection of ethionine upon the mean DNA (●) and amylase (O) activity in the sera of 3 dogs. Vertical lines through each point represent the standard deviation, while the statistical upper limit of normal for each enzyme is indicated by arrows.

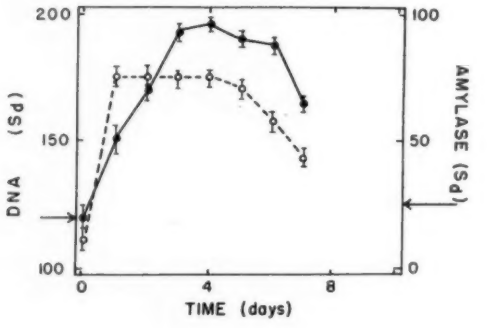

Fig. 6.

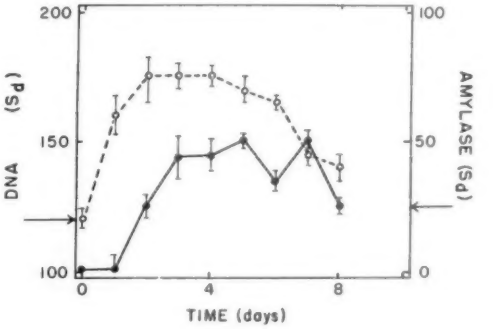

Fig. 7.

Fig. 6.—The effects of an intraluminal injection of bile prior to the ligation of the major pancreatic duct upon the mean DNA (●) and amylase (O) activity in the sera of 3 dogs. Vertical lines through each point represent the standard deviation, while the statistical upper limit of normal for each enzyme is indicated by arrows.

Fig. 7.—The effects of an intraluminal injection of bile and trypsin prior to the ligation of the major pancreatic duct upon the mean DNA (●) and amylase (O) activity in the sera of 3 dogs. Vertical lines through each point represent the standard deviation, while the statistical upper limit of normal for each enzyme is indicated by arrows.

with a subsequent abrupt return to normal. In each of the dogs the serum amylase activity remained within normal limits (Fig. 5). Clinically the dogs manifested the usual picture of lethargy and anorexia as well as gastrointestinal bleeding. At autopsy each gland showed large petechial hemorrhages, but these were located largely at the periphery and were not characteristic of the pathology of hemorrhagic pancreatitis. No ductal involvement was noted. The pathologic findings in the liver and the intestinal tract corresponded to those described elsewhere.[2] Microscopically a minimal amount of fibrosis and congestion was seen through the cut section (Table I).

Intraluminal Injection of Bile and Ligation of the Duct.—Fig. 6 shows a marked rise in the circulating concentration of both DNA and amylase activity in all 3 preparations. Each gland on gross examination was seen to be hemorrhagic, thickened, and fibrotic. The histopathologic sections revealed intraparenchymal hemorrhage, necrosis, and early organization as well as some fibrosis in all of the material (Table I).

Intraluminal Injection of Bile and Trypsin and Ligation of the Duct.—Very little difference exists between the results of this and the previous experiment. As indicated in Fig. 7, a rise in the serum levels of both DNA and amylase activity is seen. On gross pathologic examination each gland was hemorrhagic and fibrotic. Microscopic sections showed intralobular hemorrhage, necrosis, and organization (Table I).

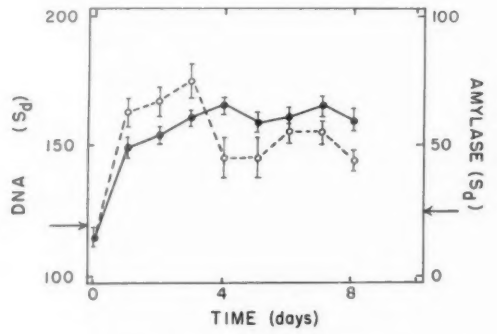

Fig. 8.—The effects of the Schwartzman reaction upon the mean DNA (●) and amylase (O) activity in the sera of 3 dogs. Vertical lines through each point represent the standard deviation, while the statistical upper limit of normal for each enzyme is indicated by arrows.

Schwartzman Phenomenon.—In all 3 preparations both serum DNA and serum amylase activities showed a substantial elevation above normal (Fig. 8). On gross pathologic examination each pancreas appeared normal. The microscopic sections showed a marked response to injury, however, with extensive hemorrhage, inflammation, edema, necrosis, and organization (Table I).

DISCUSSION

Pancreatic Peritoneal Fistula.—The pancreas was not involved in the pathologic process. Because the pancreatic secretions drained freely into the peritoneal cavity through the dangling duct, all of the tissue with which the secretions came in contact became necrotic. It is felt that the rise in

serum amylase was not a manifestation of the intrinsic pancreatic disease as in the following methods, but merely a reflection of the absorption of the enzyme across the peritoneum.

Ligation of Both Pancreatic Ducts.—Mechanical obstruction of the usual exocrine outflow of pancreatic juice in the face of a normally-secreting gland will necessarily result in an increase in the intraductal hydrostatic pressure. This in turn is reflected throughout the involved ductal system to the acini so that the usual acinus-capillary cell membrane permeability may be changed. As a result of this change it is possible that an increase in the absorption of amylase (as well as other pancreatic enzymes) by the blood may occur. When the hydrostatic pressure had increased to the point where it would mechanically cause a physiologic atrophy, the exocrine function of the cells would be decreased. The ultimate effect of this process would be pressure atrophy of all the cells which eventually empty into the ductal systems involved. Histopathologic study substantially supports this thesis.

We recorded no change in the serum DNA levels. Our results differed significantly from those of Kowlessar and McEvoy[15] who showed an initial elevation of DNA activity after ligation of the pancreatic duct in dogs.

Intraparenchymal Injection of Trypsin.—It is generally accepted that the destructive process of pancreatitis is the result of the passage of activated enzymes from the ducts into the pancreatic parenchyma. The liberated lipase and trypsin produce a digestion of fat and protein in and around the gland with resulting edema and necrosis.[7] The elevated serum DNA level would seem to be a reflection of pancreatic breakdown, whereas no hyperamylasemia was noted.

Intraperitoneal Injection of Ethionine.—Ethionine is the ethyl counterpart of methionine, an essential amino acid. As such it acts as a competitive inhibitor of methionine in its metabolic activity.[18] In view of the dynamic activity of pancreatic tissue, it is conceivable that interruption of the synthetic process in this gland by an inactive substitute (ethionine) would result in cellular degeneration.[13]

Popper[16] feels that the most important etiologic factor in pancreatitis is protein deficiency. Ethionine is a substance which inhibits protein synthesis, thereby allowing study of deficiencies of this material in the pancreas.[18]

Although our results support the hypothesis of pancreatic breakdown in this manner, they do so with meager evidence (Fig. 5). Kowlessar and McEvoy,[15] however, showed a marked increase in serum DNA levels in ethionine-treated rats.

Intraluminal Injection of Bile and Ligation of the Duct.—In 1919 Archibald[3] injected bile into the pancreatic duct of a dog and the pancreas responded with hemorrhage and necrosis. The early appearance of hypermia of the gland after injection of bile suggests that bile is a primary pancreatic irritant. Ireneus[12] noted that the severity of the pancreatitis produced in this manner depended upon the concentration of the bile.

We were able to support the findings of both Archibald and Ireneus in our experiments. The histopathologic studies show evidence of primary pancreatic injury and also ductal obstruction. These findings were reflected in the serum of all of the animals studied by a rise in both the amylase and DNA activities (Fig. 6).

Intraluminal Injection of Bile and Trypsin and Ligation of the Duct.—Kheedroo[14] was able to consistently produce acute hemorrhagic pancreatitis in dogs by injecting bile and trypsin into the main pancreatic duct and subsequently ligating the duct. Trypsin was intended to provoke vascular necrosis. Histopathologic studies in our dogs in whom this method was used revealed the expected pancreatic necrosis and obstructive sequelae resulting in a rise in both the amylase and DNA. The elevation in the latter, however, was less marked than in the previous experiment. Here trypsin may have either activated the antitryptic factors which are normally available and thus inhibited the proteolysis of the gland tissue, or the trypsin may have digested some of the DNA itself.

Schwartzman Phenomenon.—Schwartzman in 1928[17] proposed a phenomenon of local tissue reactivity. Subsequently other investigators have shown that when a suitable bacterial toxin was injected into various tissues, followed 24 hours later by an intravenous injection of the toxin, a characteristic reaction of hemorrhage and necrosis resulted. The Schwartzman reaction is essentially vascular in nature and the necrosis is a secondary phenomenon occurring as a result of capillary and venular thrombosis and hemorrhage.[21] It is used to simulate the allergic pathogenetic hypothesis of acute hemorrhagic pancreatitis.

Thal and Brackney[20] felt that the lesions seen in the Schwartzman phenomenon had a striking similarity to those seen in hemorrhagic pancreatitis and were able to produce this condition successfully and quite consistently in rabbits and goats.

We are able to show a substantial rise in both the serum amylase and serum DNA activities in dogs with pancreatitis produced by the Schwartzman phenomenon. Histopathologically, clear evidence of tissue necrosis as well as ductal obstruction is apparent (Table I).

SUMMARY AND CONCLUSIONS

Seven methods of producing pancreatitis were utilized in the experimental laboratory. Each animal was closely observed for at least 7 days, during which time daily serum analyses were made for amylase and desoxyribonuclease (DNA) activity.

In those methods in which ductal obstruction was effected, a rise in serum amylase was observed. When necrosis of the pancreas was produced by other procedures (ethionine and intraparenchymal injection of trypsin), a consistant elevation in serum DNA activity was recorded. Finally, when both ductal obstruction and pancreatic necrosis was produced by several

other methods (intraductal injection of bile and ligation, intraductal injection of bile and trypsin and ligation, and the Schwartzman reaction), elevations in both the serum amylase and serum DNA activities were measured.

From these results as well as the histopathology we conclude that obstruction of the pancreatic ductal system may be wholly responsible for the rise in serum amylase activity, while elevations in serum DNA activity were solely associated with necrosis of pancreatic parenchyma.

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THE USE OF HYPOTHERMIA WITH CARDIOPULMONARY BYPASS FOR OPEN HEART SURGERY

An Experimental Study

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THE use of hypothermia in conjunction with cardiopulmonary bypass for open heart surgery has been controversial. Clinical evidence has been unsatisfactory because of the uncontrolled nature of the observations. Previous experimental work done in our laboratory indicated that the addition of hypothermia to cardiopulmonary bypass with a bubble oxygenator greatly improved the over-all results.[1] It seemed desirable, therefore, to extend this work to study the combination of hypothermia and cardiopulmonary bypass with a rotating disc oxygenator.

METHODS

Mongrel dogs weighing 14 to 24 kilograms were used. Anesthesia was induced and maintained with intravenous thiopental sodium. Respirations were controlled by intermittent insufflation of 100 per cent oxygen into an endotracheal tube. A thermistor was inserted into the mid-esophagus for temperature measurement. The body temperature was maintained near normal in one group of animals. In the other, it was lowered to 29° to 31.5° C. This was accomplished by placing the animals in a cold ice water bath until the esophageal temperature was lowered to approximately 33° C. They were removed from the bath then and the temperature usually fell to the desired level of approximately 30° C. At the end of the experiment, the dogs were warmed by immersion in warm water. The operations were performed under nonsterile conditions. At the end of the procedure aqueous procaine penicillin, 300,000 units, was given. The chest was opened through the right fourth intercostal space. Heparin, 1.5 mg. per kilogram of body weight, was given just before the vena caval catheters were inserted. The superior and inferior venae cavae were cannulated through the right atrial appendage with large plastic catheters. One femoral artery was cannulated for measurement of the arterial blood pressure and the other for use with the pump-oxygenator. Cardiopulmonary bypass was begun and the right ventricular wall was incised. The right ventriculotomy was kept open for 30 minutes. It was closed with silk sutures. The total length of time the cardiopulmonary bypass was continued was one hour. After closure of the

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chest, a large plastic tube was inserted into the thoracic space for aspiration of air or fluid. The tube was removed 4 to 6 hours following operation. The dogs were weighed before and after operation and blood was transfused if the body weight indicated that blood loss had occurred. After the vena caval plastic catheters were removed, protamine sulfate was given to neutralize the heparin. The arterial blood pressure was measured with a U tube of mercury. A Kay-Cross rotating disc oxygenator and Sigmamotor pumps were used. When the cardiopulmonary bypass was begun, blood was allowed to drain by gravity into a reservoir placed about 30 cm. below the level of the operating table. From this reservoir blood was pumped into the oxygenator. Oxygenated blood was removed from the other end of the oxygenator and pumped into the femoral artery. Coronary and thebesian blood was aspirated into a plastic reservoir from the right ventricle by constant low-pressure suction. This was maintained at 20 mm. Hg. The oxygen saturation of the blood leaving the oxygenator was determined in some animals by the Roughton-Scholander method.

RESULTS

Cardiopulmonary bypass was carried out on 15 animals with normal body temperature and on 8 hypothermic animals (Table I). In the normothermic group, the pump flow varied from 70 to 100 c.c. per kilogram per minute. Three were perfused at 70 c.c. per kilogram per minute, and all survived over a week and were sacrificed. About 200 c.c. of bloody fluid drained from the chest in the early postoperative period. Three were perfused at 80 c.c. per kilogram per minute with only one survival. Two died within 24 hours. The surviving animal required 350 c.c. of blood in the first few hours following the operation for replacement of chest drainage. Eight were perfused at a rate of 90 c.c. per kilogram per minute. Six survived and two died within a few hours after operation. An average of 450 c.c. of blood was required to replace bloody drainage from the chest. One was perfused at 100 c.c. per kilogram per minute. It lived over a week. During the immediate postoperative period, transfusion of 560 c.c. of blood was necessary to replace the blood lost from the chest. All

TABLE I

NUMBER OF DOGS	PUMP FLOW (C.C./KG./MIN.)	AVERAGE BLOOD PRESSURE DURING BYPASS	DEATH IN 24 HOURS	SURVIVED ONE WEEK OR MORE	AVERAGE AMOUNT OF BLOOD REPLACEMENT
		Normothermia			
3	70	110	0	3	200 c.c.
3	80	103	2	1	350 c.c.
8	90	110	2	6	450 c.c.
1	100	130	0	1	560 c.c.
15			4	11	
		Hypothermia			
3	35	88	1*	2	0
2	40	95	0	2	0
2	50	81	0	2	0
1	60	80	0	1	0
8			1	7	

*Bled into pump before bypass started.

of the deaths occurred in the first 24-hour period. Autopsies revealed large amounts of blood in the chest and it was our impression that blood loss was one and probably the principal factor leading to death.

In the hypothermic group the rates of perfusion varied from 35 to 60 c.c. per kilogram per minute. Seven survived for over a week and then were sacrificed. The single death was apparently caused by a technical error. The arterial inflow tubing was inadvertently not occluded and the animal bled a large part of its blood volume into the oxygenator before cardiopulmonary bypass was begun. As a group, the amount of bloody drainage from the chest was negligible. Blood loss from chest drainage was such a small problem in the hypothermic group that in the latter part of the series no tube was inserted into the chest. No blood transfusions were necessary during the postoperative period. Ventricular fibrillation was not observed either before, during, or after operation. Most of the animals tolerated the procedure exceedingly well and were active and alert on the first day after operation.

The arterial blood pressures during the time of bypass were moderately below control levels in both groups. The oxygen saturation of the blood leaving the oxygenator was satisfactory.

DISCUSSION

This study supports the thesis that the hypothermic animal tolerates cardiopulmonary bypass with a pump-oxygenator better than the normothermic. Under the conditions of this experiment, cardiopulmonary bypass of a duration of one hour resulted in a 26 per cent mortality in the normothermic group. All of the deaths occurred within the first 24-hour period and were presumably largely a result of severe postoperative bleeding from the chest wall and operative site. It is likely that, had the period of close observation and postoperative care been extended to include 12 or 24 rather than the first 4 hours, a greater number of survivors would have been obtained. Those that survived ate and drank well on the first day after operation; however, they did not walk about the cage and, in general, were quite inactive in the early postoperative period. Although the over-all results in the normothermic animals were reasonably satisfactory, there was no question but that the hypothermic animals did better. The only death that occurred in this group was probably due to a technical error. They required little or no postoperative care. Indeed, in most instances, the animals received no special care following warming. They awakened quickly. In some instances they walked a few hours after operation, and in practically every case they were active on the first postoperative day. In comparison, the normothermic animals usually appeared more sluggish and ill at a similar time after operation.

Those animals which were operated upon at normal body temperature demonstrated a bleeding tendency in the postoperative period which contributed to the morbidity and mortality of this group. The hypothermic group was distinctly different. Hemostasis after warming was excellent and blood replacement for chest drainage was not necessary. That the hypothermic group would

bleed less than the normothermic was unexpected and was in contrast to the bleeding tendency which has often been reported following inflow occlusion under hypothermia.

The results of this study agree well with the earlier report from this laboratory in which a comparison was made between normothermic and hypothermic dogs subjected to cardiopulmonary bypass with a bubble oxygenator.

SUMMARY

Hypothermic dogs tolerate cardiopulmonary bypass with a rotating disc oxygenator better than those at normal body temperature.

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SERUM TRANSAMINASE PATTERNS FOLLOWING INTRACARDIAC SURGERY

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GLUTAMIC oxaloacetic transaminase (GOT) is a specific enzyme which catalyzes the transfer of the alpha amino group of aspartic acid to alpha ketoglutaric acid, resulting in the synthesis of glutamic acid and oxaloacetic acid.[7] The enzyme is prevalent in all animal tissues, but its activity is greatest in heart muscle, skeletal muscle, brain, and liver.[2]

The serum glutamic oxaloacetic transaminase (SGOT) activity has become a useful laboratory adjunct in the diagnosis of cardiac and hepatocellular disease, for a definite correlation has been demonstrated between the extent of myocardial or hepatic damage and the SGOT concentration.[14, 17] Experimentally SGOT has been shown to be an extremely sensitive index of hepatocellular integrity.[14]

Because of the close correlation between myocardial necrosis and SGOT levels, a study of 33 patients undergoing intracardiac surgery was undertaken. There were 10 patients with ventricular septal defects, 9 patients with tetralogy of Fallot, 9 open heart cases with perfusion but without ventriculotomies, and 5 patients undergoing closed intracardiac surgery. All 28 open heart operations were carried out utilizing the helix reservoir bubble oxygenator and Sigmamotor pump for cardiac bypass.[4] All operations were performed through bilateral transsternal thoracotomy incisions except where otherwise indicated. Patients 1, 13, and 17 were perfused via the subclavian artery, while the femoral artery was utilized for all others. Blood samples were drawn preoperatively, immediately postoperatively, and at daily intervals for at least one week. The serum was separated and stored at 0° C. All analyses were performed by the method of Karmen, Wroblewski, and LaDue,[9] as modified by Steinberg and Ostrow.[3, 20] Table I lists the mean SGOT values of the first 3 postoperative days, the patient's weight, the rate and duration of perfusion, the length of induced asystole, and the postoperative plasma hemoglobin.

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VENTRICULOTOMY

All ventricular septal defects were closed by interrupted stitches or by suturing a compressed Ivalon patch to the rim of the defect.[21] The patients with tetralogy were corrected by the insertion of a compressed polyvinyl (Ivalon) patch into the ventricular septal defect, resection of infundibular muscle, and, when indicated, the insertion of an elliptical laminated polyvinyl-Teflon roof into the right ventricular outflow tract.[10]

TABLE I

	MEAN SGOT (P.O. 1-3 U./ML.)	WEIGHT (KG.)	DURATION OF FLOW (MIN.)	FLOW (ML./KG./MIN.)	ARREST (MIN.)	PLASMA HEMOGLOBIN (MG./ML.)	REMARKS
Ventricular septal defects							
1.	182	13.3	21.0	49	—	54	Subclavian perfusion, transient heart failure
2.	179	22.2	28.1	50	9.5	75	
3.	165	11.7	25.0	85	8.2	54	
4.	150	26.8	39.5	51	10.2	47	Ventricular fibrillation after asystole
5.	150	56.6	15.5	50	—	45	
6.	148	35.8	54.6	62	25.0	81	Ventricular fibrillation after asystole
7.	131	18.8	18.8	76	—	33	
8.	103	30.0	44.6	65	24.0	39	Midline sternotomy
9.	96	46.5	35.5	60	14.3	68	
10.	95	27.0	16.5	52	—	32	
Mean	140	28.7	30.1	60.0	15.2	52.8	
Tetralogy of Fallot							
11.	330	67.2	79.1	47	27.6	116	Anomalous right coronary artery, postoperative jaundice
12.	302	15.9	56.7	63	6.2	76	Valvar and infundibular stenosis
13.	286	14.4	18.0	65	5.5	30	Subclavian perfusion
14.	256	62.7	67.6	58	32.0	72	Valvar and infundibular stenosis
15.	201	22.2	65.5	76	28.3	60	
16.	167	28.9	27.7	70	16.3	61	
17.	145	20.8	59.2	48	—	46	Subclavian perfusion, transient heart failure
18.	125	55.4	60.0	59	22.5	91	Valvar and infundibular stenosis
19.	89	63.4	78.1	51	33.6	108	
Mean	211	39.0	59.1	59.6	21.5	73.1	
Perfusion without ventriculotomy							
20.	220	20.5	18.5	49	—	41	Right thoracotomy, atrial septal defect repair
21.	152	15.1	40.1	69	—	56	Anomalous pulmonary venous drainage
22.	127	54.2	32.5	60	—	24	Atrial septal defect repair
23.	124	34.4	15.1	51	—	13	Right thoracotomy, aortotomy, aortic valvotomy
24.	101	17.5	23.7	52	—	30	Atrial septal defect repair
25.	67	44.8	39.1	89	—	28	Right thoracotomy, insertion of prosthetic cusp for mitral regurgitation
26.	62	49.4	30.0	61	—	48	Right thoracotomy, annuloplasty for mitral regurgitation
27.	62	58.9	34.3	61	—	57	Atrial septal defect repair
28.	35	36.8	14.5	76	—	61	Midline sternotomy, pulmonary valvotomy
Mean	106	36.8	25.3	63.0	—	39.8	
Intracardiac without perfusion or ventriculotomy							
29.	117	22.0	—	—	—	—	Brock pulmonary valvotomy
30.	66	52.4	—	—	—	—	Left thoracotomy, mitral commissurotomy
31.	51	56.7	—	—	—	—	Left thoracotomy, mitral commissurotomy
32.	46	18.2	—	—	—	—	Brock pulmonary valvotomy
33.	71	49.6	—	—	—	—	Left thoracotomy, mitral exploration, transient heart failure
Mean	70	39.8	—	—	—	—	

SGOT patterns of these two groups are given in Figs. 1 and 2. It can be seen from Table I that there is no definite correlation between the SGOT levels and the weight of the patients. Patients 11 and 19, the two largest in the series, had the highest and lowest SGOT values, respectively, of all the patients undergoing ventriculotomy. It can also be seen from the table that no definite correlation exists between the duration of flow or the postoperative plasma hemoglobin levels and the SGOT concentrations. These same two patients had the longest perfusions and the highest postoperative plasma hemoglobin values. Similarly the rate of perfusion and the length of induced asystole bear no apparent relationship to the SGOT levels. Furthermore, there was no correlation between either the blood pressure or the electroencephalographic tracings during the perfusion and the SGOT concentrations. It is evident, however, that the patients with tetralogy had somewhat higher SGOT values than did the ventricular septal defect patients (Figs. 1, 2, and 4).

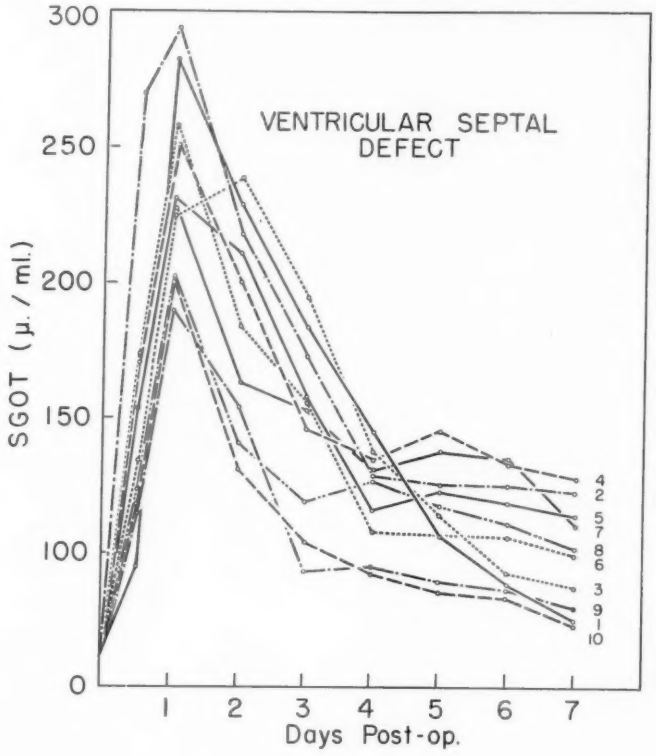

Fig. 1.

Analysis of the individual cases in relation to SGOT levels was of interest. Patient 11, whose SGOT concentrations reached 430 units/ml. on the first postoperative day, was found at surgery to have an anomalous coronary pattern over the right ventricle. The incision through the outflow tract necessarily transected some of the right ventricular blood supply. This may well have increased the amount of damage to the heart muscle. This patient also demonstrated right heart failure and concomitant jaundice; the serum bilirubin

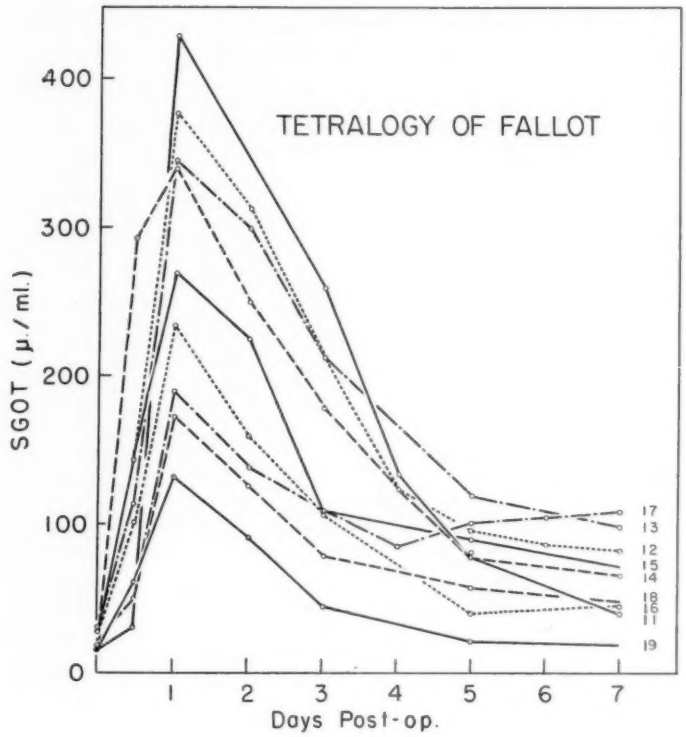
TETRALOGY OF FALLOT
SGOT (μ./ml.)
400
300
200
100
0
1
2
3
4
5
6
7
Days Post-op.
17
13
12
15
14
18
16
11
19

Fig. 2.

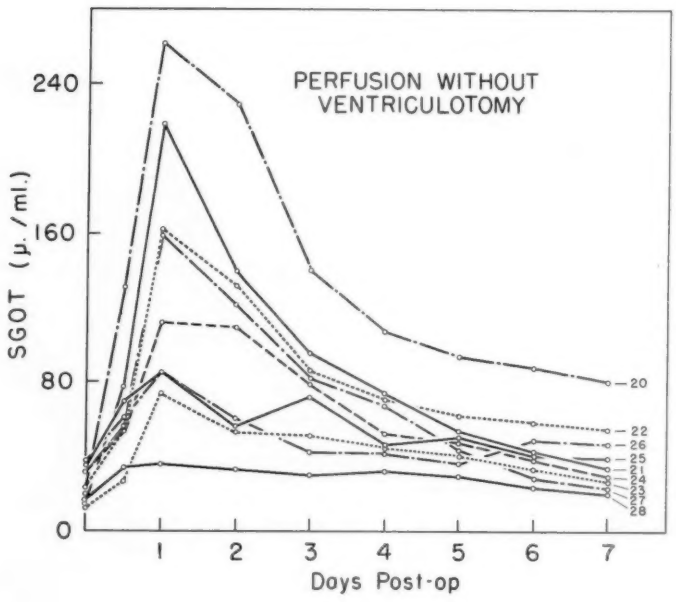
PERFUSION WITHOUT
VENTRICULOTOMY
SGOT (μ./ml.)
240
160
80
0
1
2
3
4
5
6
7
Days Post-op
20
22
26
25
24
23
27
28

Fig. 3.

level reached 5.3 mg. per cent. Liver function tests at this time were compatible with hepatocellular insufficiency. Upon a regimen of digitalis and sodium restriction both the failure and the jaundice subsided on the fourth postoperative day. There was also a simultaneous fall in the SGOT level.

Patient 17 developed signs of right heart failure on the fourth postoperative day and her SGOT level, which had been declining, began to rise. Although she demonstrated no signs of hepatic insufficiency at this time, SGOT values continued to rise until the ninth postoperative day. At this time failure had begun to subside. Patient 1 also developed transient right heart failure but she did not show an increase in SGOT level. There was no electrocardiographic evidence of myocardial infarction in any of the patients, and neither laboratory nor clinical evidence of hepatic insufficiency was present in any patient except Patient 11.

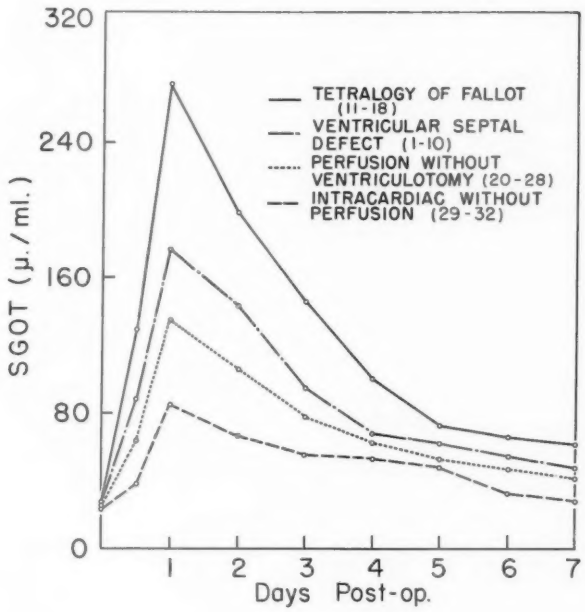

Fig. 4.

Patient 8 was the only patient undergoing a ventricular incision through a midline sternotomy. SGOT levels were less than those of the majority of patients subjected to bilateral thoracotomies and ventricular incisions. The smaller amount of skeletal muscle injury resulting from the midline sternotomy may well account for this difference.

PERFUSION WITHOUT VENTRICULOTOMY

Patients 20 through 28 underwent total body perfusion for nonventricular open heart surgery. The patients in Cases 20, 22, 24, and 27 had atrial septal defects repaired by the insertion of interrupted silk sutures tied over Ivalon pledgets through a right atriotomy. The reason for the variations in their postoperative SGOT concentrations is not apparent. for there is no correlation

between their perfusion data and their SGOT values. Patient 21 was operated upon for repair of anomalous pulmonary venous drainage into the right atrium. A defect in the atrial septum was created for the correction, and this may have contributed to SGOT values. The patients in Cases 25 and 26 were operated upon through right thoracotomies for correction of mitral regurgitation.[12] Both were adults in severe heart failure (Class IV) who underwent extracorporeal circulation for periods of 39 and 30 minutes. However, both their postoperative SGOT concentrations reached a maximum of only 84 units/ml. Patient 28 underwent a midline sternotomy and a 14.5-minute cardiac bypass for pulmonary stenosis. His postoperative SGOT levels were the lowest in the series, lower than any of the nonperfusion cases, reaching a maximum of only 36 units/ml. (preoperative value—16 units/ml.).

INTRACARDIAC WITHOUT PERFUSION

Cases 29 through 33 represent patients who had closed intracardiac operations without cardiac bypass. Cases 29 and 32 underwent Brock procedures through bilateral transsternal thoracotomies. The reason for the high SGOT levels in Patient 29 is not apparent, for he had a completely uneventful postoperative course. The patients in Cases 30 and 31 had mitral commissurotomies through left thoracotomies and showed minimal SGOT elevations. Patient 33 underwent left thoracotomy and left atriotomy for mitral disease. However, she was found to have almost pure regurgitation and the incision was closed. She developed heart failure on the third postoperative day. SGOT levels began to rise and reached a value of 217 units/ml. on the fifth postoperative day. SGOT values then declined as heart failure subsided. Although she had moderate hepatomegaly, all liver function tests at that time were normal. She subsequently underwent total body perfusion and successful annuloplasty for repair of the mitral regurgitation, but unfortunately SGOT specimens were not obtained.

DISCUSSION

It has been shown both experimentally and clinically that SGOT concentrations are increased predominantly by stress or injury to cardiac muscle, skeletal muscle, or liver.[1, 4, 15, 17] Skeletal muscle incision undoubtedly contributed some SGOT, but from our data and other studies it seems that bilateral transsternal thoracotomy and pericardiotomy might raise the SGOT levels only to 60 to 80 units/ml.[1, 15, 19]

The ventriculotomy probably also released GOT into the circulation, for there was a mean difference on the first postoperative day of 40 units/ml. between the patients with ventricular septal defects and the patients who were perfused but did not have ventriculotomies. The significance of postoperative pericarditis in relationship to SGOT levels is not known but is probably a significant factor, for increased values are reportedly found in 0 to 75 per cent of patients with isolated pericarditis.[11] Most patients undergoing thoracotomy have a certain amount of associated pneumonitis postoperatively and the possibility that the lungs may have contributed to these elevations of SGOT

observed has been considered. However, this does not seem likely since even in the presence of pulmonary infarction normal SGOT levels were observed in 6 of 7 patients.[16]

The effect of total body perfusion during cardiac bypass on the SGOT concentrations is less clear. Possibly the atriotomies for insertion of the caval catheters contribute small amounts. Also hemolysis during cardiac bypass would tend to raise the SGOT levels.[13] However, the low levels in Cases 25, 26, 27, and 28 would indicate that perfusion per se, even when combined with a major intracardiac procedure, need not elevate the SGOT values.

Nyhus[18] has stated that the isolated liver tolerated perfusion poorly, developing severe edema, under the conditions of his study. It is possible that extracorporeal circulation might subject the liver to reduced oxygenation, edema, or passive congestion of a degree sufficient to cause it to release GOT. This change need not be severe, for SGOT is known to be an extremely sensitive index of hepatocellular integrity, and values up to 28,000 units/ml. have been demonstrated in reversible liver damage.[14] Moreover, Poulk and Fleisher[6] have shown that a single dose of codeine phosphate in some patients may cause very large elevations of SGOT. From this they concluded that while it was probable that the opiate acted through effects on the liver or biliary tract, it was unlikely that necrosis of liver cells was necessary to produce high levels of SGOT. We have made no detailed attempt to assess the possible influence of opiates, but the children, in this study, in only rare instances received any sedation postoperatively, whereas most of the adults received small doses of Demerol during the first 48 hours.

Many patients who have previously been or are in cardiac failure probably have passive congestion of their livers or even subclinical centrilobar necrosis which could be accentuated by extracorporeal circulation. DuToit[5] demonstrated increased SGOT levels in 16 of 23 patients in uncomplicated congestive failure and he postulated centrilobar necrosis as the source. This may well have contributed to the SGOT values in Cases 11, 17, and 33.

The explanation for the differences between the SGOT levels of the patients with tetralogy and ventricular septal defects is probably related to differences in their pathologic physiology and anatomy. From the mean values it can be seen that the patients with tetralogy were larger and their perfusions of longer duration. However, analysis of the individual cases fails to reveal any constant correlation. The length of the cardiotomy incisions was approximately the same in both groups and there was no preponderance of right ventricular hypertrophy in the patients with tetralogy compared to those with ventricular septal defects.

One probable factor may be accounted for by the extensive bronchial circulation of the patients with tetralogy. This serves as a run-off from the perfusion, for as much as 1,500 ml. per minute can be withdrawn via the cardiotomy suction in the right heart.[8] This could render the distal perfusion less effective and consequently could cause the liver to be less adequately perfused. The infundibular resection would appear to be of some consequence,

for considerable cardiac muscle is excised. However, the right ventricular outflow tract repair (prosthetic roof) would not seem likely to increase the SGOT values for it entails little, if any, additional trauma to the myocardium.

SUMMARY

Thirty-three patients undergoing intracardiac surgery were followed with daily SGOT levels for one week. Twenty-eight patients had total body perfusions wth open intracardiac procedures. Five additional patients having intracardiac procedures without perfusion served as controls. Although perfusion did not raise the SGOT concentrations in all patients, it seemed to be a contributing factor in most cases. However, the lowest value observed in the entire series was in a patient having total body perfusion. The patients with tetralogy of Fallot had greater postoperative levels than those with ventricular septal defects. This difference could be related to the physiologic and anatomic abnormalities peculiar to this malformation. SGOT values were greater in patients undergoing perfusion and ventriculotomy than those subjected to perfusion and nonventricular cardiotomies. Hepatic changes during perfusion are suggested as the major source of these increased SGOT values but obviously many other organs and tissues may contribute.

If SGOT levels can be regarded as a sensitive index of tissue integrity as has been suggested by numerous studies, then it may be concluded that a properly conducted total body perfusion with an efficient pump-oxygenator has maintained bodily homeostasis remarkably well during the temporary intervals studied.

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PROPHYLACTIC TREATMENT OF THE MURPHY STURM RAT LYMPHOSARCOMA WITH NITROGEN MUSTARD

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IN 1955 Cruz and associates[1] reported that when nitrogen mustard was given to rats one minute after inoculation of Walker 256 cells into a branch of the portal vein, the takes were decreased considerably below the percentage sustained by control animals inoculated with the same number of cells and by the same route. Since then Thomas and associates[5] have reported that the "takes" of Ehrlichs mouse adenocarcinoma cells when injected intraperitoneally or subcutaneously are decreased by various chemotherapeutic agents when the drug is given before the cells attain the "invasive" state.

To test out the prophylactic effect still further we considered it advisable to try a tumor which was comparatively resistant to treatment with anticancer agents.

Murphy and Sturm[7] induced a leukemia in rats with 1,2,5,6 dibenzanthracene. Among the animals that had been injected subcutaneously with leukemic cells, they found two that had developed a lymphosarcoma at the site of inoculation. In further studies[6] they proved this tumor to be easily transplantable and rarely spreading beyond the regional lymphatics. On the other hand they found that when this tumor was inoculated intraperitoneally the original leukemia was reproduced. Heidelberg and Baumann[2] found OPSPA highly effective against this lymphosarcoma, while Suguira and Stock[8] found that methyl bis (beta chlorethyl) amine oxide, in daily doses of 1.5 mg. per kilogram of body weight, had no inhibitory effect. The latter investigators also found phosphoramide compounds (SK3818 and SK4614) had no growth inhibitory effect. Since so many anticancer agents failed to inhibit the growth of the Murphy Sturm tumor, this tumor was chosen for testing with the prophylactic technique previously reported.

METHOD

A cell suspension of the Murphy Sturm lymphosarcoma was prepared using the technique described by Lucke and associates.[3] Aseptic technique was used for preparation of the cells and during the operation we made a suspension of 200,000 cells in 1 ml. of saline and injected this amount intraportally (into a

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branch of the portal vein) in 100 rats. To 62 of these rats we gave 0.5 mg. nitrogen mustard per kilogram of body weight intraportally within one minute after the cell suspension was injected; the other 38 rats were used as controls. We repeated the experiment injecting 500,000 cells. Animals dying within 96 hours of operation were excluded from the experiment. The time of death of the rats in both groups was recorded, and microscopic sections were taken in 32 consecutive cases to confirm the cause of death.

RESULTS

In the group inoculated with 200,000 cells, 80 per cent (30) of the control animals died between 7 and 32 days, whereas only 48.6 per cent (30) of the treated animals had died by the end of that period. The surviving animals were observed for an additional 2 months, but none died.

In the group inoculated with 500,000 cells 85.1 per cent (27) of the control animals died within 22 days after inoculation, whereas only 62.8 per cent (35) of the treated animals had died up to the end of that period. All surviving animals were observed for an additional period of 2 months but none died.

In the group inoculated with 500,000 cells, microscopic sections of the liver and spleen were studied after death in 16 consecutive treated animals and in 16 consecutive control animals. We considered this necessary since the gross diagnosis of the Murphy Sturm tumor is not made as readily as it is in many other tumors, such as the Walker 256 carcinosarcoma. In the treated group satisfactory sections were unobtainable in two because of cannabalism and putrefaction; this left 14 for diagnosis. Of the 14 treated animals a diagnosis of leukemia or lymphoma was made in 13 (93 per cent); diagnosis in the fourteenth animal was inconclusive. In the 16 control animals a diagnosis of leukemia or lymphoma was made in 14 (87.5 per cent); in the other 2 animals the diagnosis was inconclusive. If these animals lacking confirmatory microscopic diagnosis were excluded, it would affect the final figures very little.

DISCUSSION

When 200,000 cells were inoculated into the portal system and 0.5 mg. nitrogen mustard per kilogram of body weight was given within one minute (also into a branch of the portal vein), the takes or deaths were reduced from 80 per cent in the control animals to 48.3 per cent in the treated animals. This is statistically significant.

When 500,000 cells are inoculated into the portal system and 0.5 mg. nitrogen mustard per kilogram of body weight was given within one minute after the cells, takes were reduced from 85.1 per cent in the control animals to 62.8 per cent in the treated animals. This is not statistically significant. It is well known that massive cell doses and massive tumors are comparatively resistant to drug therapy. Accordingly, we would not expect the nitrogen mustard to be as effective in this group receiving 500,000 cells, but the difference is large enough perhaps to indicate a trend.

In some work just completed in this laboratory and being prepared for publication, we have noted that when Walker 256 cells are given subcutaneously

(instead of intraportally) nitrogen mustard is not very effective in preventing takes. Since the Murphy Sturm tumor is not inhibited as much as the Walker 256 tumor by giving nitrogen mustard shortly after inoculation of the cells, we would not expect the Murphy Sturm tumor to be significantly inhibited if the cells were given subcutaneously.

SUMMARY

We injected 200,000 Murphy Sturm tumor cells into a branch of the portal vein of 100 female Sprague Dawley rats; to 62 of this group 0.5 mg. nitrogen mustard per kilogram of body weight was given into the same vein within one minute after inoculation of the cells. The rest (38) were used as controls. Eighty per cent of the control animals died whereas only 48.3 per cent of the treated animals died. When we repeated the experiment with injection of 500,000 cells, 85.1 per cent of the control animals died, and 62.8 per cent of the treated animals died. The nitrogen mustard was less effective in reducing takes and death following injection of the large number of cells and is to be expected since it is well known that a massive number of cells or massive tumors are comparatively resistant to drug therapy.

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METHODOLOGIC AND ACTUAL ERROR OF PLASMA VOLUME DETERMINATION

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DETERMINATION of the blood volume has been used on our surgical services in the clinical evaluation of patients who have had acute or chronic loss of circulating blood volume. Because the estimation of the total blood volume is especially important in these patients, it is necessary to know the limitations of the various methods of determining volume. This study has been undertaken to determine the limitations in the use of Evans blue dye (T-1824) and of RISA under control conditions and in various physiologically abnormal conditions. The results obtained with T-1824 and with RISA were compared by administering them to the same patients simultaneously. We have also compared the accuracy of plasma volume determination by using a single 10-minute sample and by using the extrapolation technique with three or more samples.

In an attempt to define the accuracy of the estimation of plasma volume, both the accuracy of the method itself (methodologic[22] or technical[28] error) and the accuracy of the method as applied to a number of patients (actual or biologic error[28]) must be determined.

Methodologic error is defined as the standard deviation of an observation calculated from experiments in normal subjects in which the observation is repeated twice in direct succession (intrapatient variation). The standard deviation of the differences of these two determinations ($s\Delta I, II$) is the error of the method, and in the case of the T-1824 method of measuring plasma volume includes the variation in injection, sampling, mixing, color of the plasma, hemolysis, and lipemia. With the use of RISA, variation in injection and in sampling and the errors of isotopic counting are the determining factors. Thus, the methodologic error indicates the reliability of the method under ideal conditions.

The actual (*biologic*) error combines patient differences with methodologic error (interpatient variation). In the determination of plasma volumes, the actual error consists of such patient-to-patient variations as mixing of the plasma tag, capillary permeability, and the extravascular uptake of the tag. The components of the actual error are not factors which account for differences when determinations are repeated in the same individual but account for variations between individuals. This biologic variation cannot be measured directly. However, it is possible to estimate the magnitude by analyzing the variation in a series of determinations and to consider it in clinical situations.

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METHODS OF DETERMINING PLASMA VOLUME AND CALCULATING ERROR

T-1824 Tag.—A control sample of venous blood is drawn and a known amount of T-1824 is injected. At 10, 20, and 30 minutes post injection, blood samples are drawn from the opposite extremity. All samples are heparinized and drawn without stasis. An hematocrit determination is made on each sample and the remainder of the blood is centrifuged for 10 minutes at 3,000 r.p.m. The plasma is then removed and centrifuged for an additional 30 minutes at 3,000 r.p.m. The optical density of the plasma is measured on a Coleman spectrophotometer.

Ten-minute volumes: The concentration of the 10-minute sample is used in the dye dilution formula.

Extrapolated volumes: The density of the 3 samples is plotted against time and a straight line (arithmetic mean of the points) is extrapolated to estimate the "zero time" density. A calibration curve gives the "zero time" dye concentration.

$$\text{The calculations:}\quad \text{Plasma Volume} = \frac{\text{c.c. dye injected} \times 5000^{*}}{\text{Gm. dye per c.c. at "zero time" (or 10 min.)}}$$

$$\text{Blood Volume} = \text{Plasma Volume} \times \left[\frac{100}{100 - \text{Hmct.}^{\dagger}}\right]$$

RISA Tag.—A known amount of radioactive iodinated human serum albumin‡ is injected intravenously. At 10, 20, and 30 minutes post injection, blood samples are drawn from the opposite extremity. All samples are heparinized and drawn without stasis. Hematocrit is determined on each sample and corrections are applied to the counts if the hematocrits vary by more than 2 per cent. The amount of radioactive iodine in each sample is determined by counting 1 c.c. aliquots of whole blood in a well-type scintillation detector with a probable counting error of 1 per cent.

Ten-minute volumes: The counts per minute (c.p.m.) of the 10-minute sample are used in the dye dilution formula:

Extrapolated volumes: The counts per minute of the 3 samples are plotted against time and a straight line (arithmetic mean of the points) is extrapolated back to zero time.

$$\text{Blood volume} = \frac{\text{c.c. RISA injected} \times \text{c.p.m. RISA standard}}{\text{c.p.m. at zero time (or 10 minutes)} \times \text{dilution of standard}}$$

$$\text{Plasma volume} = \text{Blood volume} \times (100 - \text{Hmct.})$$

Calculations of methodologic error: Subjects with no known circulatory disorders were prepared by fasting and bed rest for eight hours prior to the test. Duplicate determinations were made on each patient and the mean percentage of difference between determination plasma volume I and plasma volume II was calculated.

*A calibration factor.

†A correction (0.91)[4] for difference between total body and peripheral hematocrit is omitted for convenience because all data are compared with simultaneous data on the same patient.

‡Abbott Laboratories, Oak Ridge, Tenn.

$$d = \frac{\text{plasma volume I} - \text{plasma volume II}}{\text{plasma volume II}} \times 100 = \text{percentage of difference}$$

$$\bar{d} = \frac{\Sigma_1^n \frac{I - II}{II} \times 100}{n} = \text{mean percentage of difference}$$

$$sd = \sqrt{\frac{\Sigma_1^n (d - \bar{d})^2}{n - 1}} = \text{standard deviation of percentage of difference} = \text{methodologic error}$$

$$s\bar{d} = \frac{sd}{\sqrt{n}} = \text{standard error of mean percentage of difference}$$

$$t = \frac{\bar{d}}{sd}\sqrt{n}$$

P from Table 38; Snedecor, G. E.: Statistical Methods, Ames, Iowa, 1946, Iowa State College Press.

Calculations of actual error: Patients were grouped according to the specifications set up for each group, that is, young healthy men, routine hospital patients, and upper gastrointestinal bleeders. Where actual errors of two methods are compared, both determinations were made simultaneously on the same patient.

n = number of observations

$\bar{x}$ = mean

$$sx = \sqrt{\frac{\Sigma_1^n (x - \bar{x})^2}{n - 1}} = \text{standard deviation of } x$$

$$s\bar{x} = \frac{sx}{\sqrt{n}} = \text{standard error of } \bar{x}$$

FACTORS INFLUENCING THE METHODOLOGIC ERROR OF THE EVANS BLUE METHOD

The methodologic error with T-1824 dye has been determined by many investigators. Gibson[10] ran repeated determinations of plasma volume and found a maximum variation of 15 per cent, while Clark[6] found a 10 per cent variation in the study of 4 patients. Porat[24] ran duplicate determinations on 10 normal patients and found a standard deviation for T-1824 measurements of ±5.4 per cent. The factor which contributes most to this range of error is the optical density of the plasma, which may be altered by hemolysis and lipemia.

Experiments to Determine the Variability of Optical Density of Control Plasma.—A control sample of plasma is used as a blank to reduce errors introduced by variations in the optical density of the plasma. However, it has been noted that if one draws 2 blanks from the same patient, they will have different optical densities, presumably due to different degrees of stasis while drawing the specimen.[11] Therefore, the error introduced into the plasma volume estimation by variability in optical density of the blank was determined.

Method: T-1824 dye was used to measure the plasma volumes of 15 patients by the extrapolation technique. Two control samples were drawn (often with

the same needle in place) prior to injecting the dye; thus it was possible to calculate 2 plasma volumes using each control sample as a blank. The mean percentage of difference of volumes I and II and the standard deviation of this percentage of difference were calculated.

Results: The mean percentage of difference between the 2 plasma volumes was –4.5 per cent with a standard deviation of ±16.2 per cent (range: –32.6 to +35.1 per cent) (Table I).

TABLE I. REPRODUCIBILITY OF PLASMA VOLUME AS INFLUENCED BY VARIATION IN OPTICAL DENSITY OF CONTROL PLASMA

n	$\bar{d}$	RANGE	sd	$\overline{sd}$	t	p
15	–4.5%	–32.6% to +35.1%	±16.2%	4.2%	1.07	0.3

Experiments to Determine the Influence of Lengthening Centrifugation on Reproducibility.—When we used the T-1824 and the RISA methods of plasma volume simultaneously in the same patient, the T-1824 method consistently measured larger plasma volumes although visibly hemolyzed samples were discarded and gross lipemia was not present. Blood samples were drawn without a tourniquet to avoid variations in venous stasis. Centrifuging out lipemic particles to reduce the variation in optical density of the plasma was undertaken. It was hoped that this technique might reduce the difference in plasma volume values observed. Repeat determinations were done to ascertain the effect of lengthening centrifugation on the accuracy of the T-1824 method.

Method: Two serial T-1824 plasma volumes were run by extrapolation technique in direct succession on 23 patients in a steady state.

The second determination was run by injecting a second aliquot of dye within 5 minutes of the withdrawal of the first 30-minute sample. The first 30-minute sample is the control for the second plasma volume. All 7 samples from a patient were centrifuged simultaneously for three 10-minute intervals, totaling 10, 20, and 30 minutes at 1,400 G. Optical densities were measured after each interval of centrifugation and the plasma volume was calculated by extrapolation. Thus, for each patient 6 plasma volume calculations were made. The percentage of difference of the duplicate plasma volumes centrifuged for a total of 10 minutes was determined, as well as the mean percentage of difference and the standard deviation of this mean. The same calculations were carried out for 20 and 30 minutes of centrifugation.

Results: The data which show the reproducibility of plasma volumes after 10, 20, or 30 minutes of centrifugation is tabulated in Table II. Centrifugation of the plasma for 10 minutes resulted in a mean of the difference between the 2 successive plasma volumes of 8.1 per cent and a standard deviation of this difference of ±29.6 per cent. The reproducibility improved with lengthening time of centrifugation until 30 minutes of centrifugation resulted in a mean difference of 2.5 per cent, ±14.0 per cent. Although the error of the method decreased with increasing time of centrifugation, the actual plasma volume as measured did not change.

TABLE II. REPRODUCIBILITY OF PLASMA VOLUME AS INFLUENCED BY LENGTH OF TIME OF CENTRIFUGATION

LENGTH OF TIME OF CENTRIFUGATION (MINUTES)	PLASMA VOLUME (C.C.)		COMPARISON OF DUPLICATE MEASUREMENTS ON EACH OF 23 PATIENTS					
	n	$\bar{x}$	n	$\bar{d}$	sd	$s\bar{d}$	t	p
10	46	2,738	23	+8.1%	±29.6%	±6.17%	1.31	0.2
20	46	2,857	23	+8.9%	±20.5%	±4.27%	2.08	0.05
30	46	2,768	23	+2.5%	±14.0%	±2.92%	0.86	0.4

METHODOLOGIC ERROR OF T-1824 AND RISA METHODS

In order to determine as accurately as possible the methodologic error with the use of T-1824 as compared with RISA, simultaneous repeated plasma volume determinations in the same patient were performed with these tags.

Experiments to Determine the Methodologic Errors With the Extrapolation Technique.—

Method: T-1824 and RISA were mixed in a sterile Fenwall bottle just prior to use. A known aliquot of the mixture was injected and the plasma volumes were determined as outlined previously. The second determination immediately followed the first. The third sample from the first plasma volume acted as the control for the second test. Volumes were calculated using the extrapolation technique.

To rule out patient-to-patient variations, the standard deviation of the percentage of difference of the 2 observations on the same patient was calculated. The means percentages of difference, the standard deviations, and the standard errors were calculated for both T-1824 and RISA.

Results: The results of these experiments are tabulated in Table III. It should be noted that the mean of the differences is not significantly removed from zero for both methods, but the standard deviation of the differences for the T-1824 measurement (17 per cent) is nearly triple that for RISA (6.5 per cent). Therefore, the methodologic error using T-1824 is approximately triple that for RISA.

TABLE III. DUPLICATE MEASUREMENTS OF VOLUME USING RISA AND T-1824 SIMULTANEOUSLY

	n	$\bar{d}$	sd	$s\bar{d}$	t	p
RISA	22	−0.4%	±324 c.c. (±6.5%)	±1.4%	0.29	>0.5
T-1824	22	−3.1%	±756 c.c. (±17.0%)	±3.6%	0.86	0.4

Experiments to Determine the Methodologic Error With the 10-Minute Sampling Technique.—Because of the disappearance of the plasma tag from the circulating blood and variability of mixing of the tag with the plasma, it has been postulated that variation in results of measurements of the plasma volume may be reduced by using the extrapolation technique in preference to the single 10-minute sample technique.[11, 19, 21] The reproducibility of the method using the single 10-minute sampling technique was therefore determined.

Method: The duplicate plasma volume determinations performed for the evaluation of the extrapolation technique were calculated using the 10-minute

sample only. In those instances in which the first sample was not drawn at exactly 10 minutes, this comparison was not made. The mean percentage of difference between samples I and II, the standard deviation of this mean, the standard error, and t were calculated.

Results: The reproducibility (methodologic error) of the plasma volume using the extrapolation or single 10-minute sample method is essentially the same for a particular tag (Table IV).

TABLE IV. REPRODUCIBILITY OF PLASMA VOLUME IN THE SAME PATIENT

METHOD	n	$\bar{d}$	sd	$s\bar{d}$	t	p
RISA						
Extrapolation	22	−0.4%	±6.5%	±1.38	0.29	0.5
10-minute sample	13	−1.3%	±6.6%	±1.83	0.71	0.49
T-1824						
Extrapolation	22	−3.1%	±17.0%	±3.62	0.86	0.40
10-minute sample	10	−12.6%	±15.0%	±4.75	2.78	0.02

ACTUAL OR BIOLOGIC ERROR

To evaluate the actual interpatient variation of the blood volume determination, groups of patients under varying conditions were studied. To check the "ideal" actual error and to compare our results with other published data, blood volumes were measured on normal young adult men. Male hospital patients in a steady state were studied to evaluate the average patient-to-patient variation in this heterogeneous population. Patients with a diagnosis of massive upper gastrointestinal bleeding had volumes measured immediately after admission to the hospital. An analysis of the results on those patients who showed a 40 per cent loss of their normal circulating red cell mass was used as a comparison of the agreement between extrapolated and single 10-minute sample methods for determination of blood volume of a patient with massive bleeding.

Method: RISA and T-1824 blood volumes were determined as previously outlined, using both the extrapolation and single 10-minute sample methods. Where two or more methods were compared, simultaneous studies were done so the actual errors could be calculated for identical series of patients. The mean volume in cubic centimeters per kilogram of body weight, standard error, and standard deviation of the mean were calculated according to the definitions given previously.

Results: A mean total blood volume of 69.2 c.c. per kilogram with an actual error of ±11 per cent (Table V) was found in the young healthy men. A comparison of the actual errors using T-1824 or RISA for blood volume determinations in the routine hospital patients are given in Table VI, *A* and *B*. Table VI, *B* compares both plasma tags by 2 methods on the same 22 patients and shows that the actual error is a function of the plasma tag and is not altered by the number of samples used for the calculation of the blood volume. Table VI, *A* for larger series, shows the actual error of RISA is half that of T-1824. The mean measured volume is slightly higher with RISA. The results in the

gastrointestinal hemorrhage patients (Table VII) are similar to patients in a steady state in that the 10-minute sample method was as valid as the extrapolation method. However, the blood volume obtained using the 10-minute sample is statistically significantly larger (3 per cent for RISA and 11 per cent for T-1824) than that obtained by extrapolation (Table VIII).

TABLE V. ACTUAL ERROR OF RISA METHOD IN NORMAL ADULT MEN

	n	$\bar{x}$	sx	$s\bar{x}$
Normal men	14	69.2 c.c./Kg.	±7.7 c.c./Kg. (±11.1%)	±2.06 c.c./Kg. (±3.0%)

TABLE VI

METHOD	n	$\bar{x}$	sx	$s\bar{x}$	MEDIAN
A. Actual Error of Methods: Hospital Patients With No Known Circulatory Disorders					
RISA					
Extrapolation	44	83.4 c.c./Kg.	±11.44 c.c./Kg. (±13.7%)	±1.72 c.c./Kg. (±2.1%)	81.8 c.c./Kg.
10-minute sample	26	88.7 c.c./Kg.	±13.86 c.c./Kg. (±15.6%)	±2.72 c.c./Kg. (±3.0%)	
T-1824					
Extrapolation	44	75.4 c.c./Kg.	±20.05 c.c./Kg. (±26.6%)	±3.02 c.c./Kg. (±4.0%)	79.7 c.c./Kg.
10-minute sample	22	76.7 c.c./Kg.	±19.03 c.c./Kg. (±24.8%)	±4.15 c.c./Kg. (±3.7%)	
B. Comparison of the 4 Methods Simultaneously on the Same Patient					
RISA					
Extrapolation	22	83.0 c.c./Kg.	±13.0 c.c./Kg. (±15.7%)	±2.8 c.c./Kg. (±3.4%)	
10-minute sample	22	86.5 c.c./Kg.	±13.2 c.c./Kg. (±15.3%)	±2.8 c.c./Kg. (±3.3%)	
T-1824					
Extrapolation	22	70.0 c.c./Kg.	±19.7 c.c./Kg. (±28.1%)	±4.2 c.c./Kg. (±6.0%)	
10-minute sample	22	76.7 c.c./Kg.	±19.0 c.c./Kg. (±24.8%)	±4.2 c.c./Kg. (±3.7%)	

TABLE VII. ACTUAL ERROR OF METHODS IN PATIENTS WITH GASTROINTESTINAL HEMORRHAGE

METHOD	n	$\bar{x}$	sx	$s\bar{x}$
RISA				
Extrapolation	56	57.7 c.c./Kg.	±11.6 c.c./Kg. (±20.1%)	±1.55 c.c./Kg. (±2.7%)
10-minute sample	56	59.8 c.c./Kg.	±12.8 c.c./Kg. (±21.4%)	±1.71 c.c./Kg. (±2.8%)
T-1824				
Extrapolation	37	63.5 c.c./Kg.	±19.1 c.c./Kg. (±30.1%)	±3.14 c.c./Kg. (±4.9%)
10-minute sample	37	73.2 c.c./Kg.	±27.0 c.c./Kg. (±36.9%)	±4.44 c.c./Kg. (±6.1%)

TABLE VIII. PERCENTAGE OF DIFFERENCE BETWEEN EXTRAPOLATION AND 10-MINUTE VOLUMES ON HEMORRHAGE PATIENTS

PLASMA TAG	n	$\bar{d}$	sd	$s\bar{d}$	t	p
RISA	56	−3.0%	±6.4%	±0.8%	3.48	<0.01
T-1824	37	−10.8%	±18.8%	±3.1%	3.48	<0.01

$$\bar{d} = \frac{\sum_1^n \frac{\text{extrap.} - 10 \text{ min.}}{10 \text{ min.}} \times 100}{n}$$

DISCUSSION

The application of the statistical "t" test to the duplicate determinations indicates (in all series of significant size) that the values for the first and second serial determinations of plasma volume were the same. Therefore, there is no indication that the duplicate determinations were affected by an error inherent in the method of the study. Presumably, all errors inherent in the use of either tag (protein loss into the lymph, dilution by tissue fluid, and so forth)[3, 7-9, 12, 14, 18, 25-27] influence each determination equally since both tags are used simultaneously and immediately consecutively in the same patient.

Our data (Table III) indicate that the reproducibility of plasma volume determinations using RISA is considerably more satisfactory than with T-1824 (±6.5 per cent versus ± 17.0 per cent).

The data for the determination of the methodologic error have been obtained by skilled technicians who do a large number of these determinations. In spite of these relatively ideal circumstances, the reproducibility of the plasma volume using the T-1824 technique was ±17 per cent.

TABLE IX. SUMMARY OF DATA

	RISA 10-MINUTE	RISA EXTRAPOLATION	T-1824 10-MINUTE	T-1824 EXTRAPOLATION
Methodologic error				
Steady state patients	±6.6%	±6.5%	±15.0%	±17.0%
Hemorrhage—10-minute vs. extrapolation	±6.4%		±18.8%	
Actual error				
Normals		±11.1%		
Steady state patients	±15.3%	±15.7%	±24.8%	±28.1%
Hemorrhage	±21.4%	±20.1%	±36.9%	±30.1%

Attempting to determine the factors which contribute to this large error, we have found that the variation in the optical density of the control sample of plasma used in the spectrophotometric determinations was ±16 per cent. The accuracy of the method is therefore limited to this range of error. This error exists despite the preliminary centrifugation of the supernatant plasma. Thirty minutes of centrifugation has been used in all our work, using optical densities of plasma, because our data indicate that prolonged centrifugation reduces the difference between duplicate determinations.

Reproducibility decreased to ±14 per cent after 30 minutes of centrifugation. Lesser periods of centrifugation result in successively higher errors, the error being 29.6 per cent for 10 minutes of centrifugation.

Prolonged centrifugation eliminates visible lipemia, but it is considerably more difficult to correct for lipemia completely. Accurate correction for lipemia may be obtained by extraction of the dye with cellulose[1, 2] or by chromatographic separation of the dye.[20] Extraction of the lipid from the plasma with acetone yields satisfactory reproducibility at the expense of higher total plasma volumes.[5] Other methods based upon lipid extraction also show loss of dye and, subsequently, higher measured volumes and are not satisfactorily reproducible. Electrophoretic studies on plasma from patients with nephrosis show large amounts

of lipoids migrating with the alpha and beta globulins.[29] Since T-1824 readily combines with globulins,[2] it is difficult to remove lipoid particles without some loss of dye. Methods based upon optical corrections for lipids[5, 16, 23, 29] are valid only at low lipid concentrations because secondary scattering of light, which does not follow the Beer-Lambert law, increases in random fashion with increasing concentration of colloidal particles and invalidates these corrections. Although prolonged centrifugation removes visible lipemia, the persisting error of ±14 per cent may be partially due to residual lipemic particles. It appears that ±14 per cent is our minimum error of reproducibility for routine determinations.

All of the samples used in this study have had no visible hemolysis. Visibly hemolyzed samples were discarded because it is not practical to make corrections for free hemoglobin. Nickerson[21] and others[23] have shown that the different heme molecules have differing spectrums, the concentrations of which vary in normal blood; therefore, corrections for free hemoglobin based upon the optical density obtained at the different wave lengths are approximately correct only at low concentrations. Phillips makes the correction for hemolysis by converting all hemoglobin to oxyhemoglobin, but the reaction time is 24 hours.[23] Only by using chromatographic separation have satisfactory in vitro corrections for free hemoglobin been accomplished.[20] Thus, it would seem that for any other than special research studies, where time may not be an important factor, visibly hemolyzed samples should be discarded.

The mean blood volumes obtained by injecting T-1824 and RISA together (Tables VI, *A* and *B*) suggests that the use of T-1824 results in a smaller total volume. The median values (81.8 c.c. per kilogram for RISA and 79.7 c.c. per kilogram for T-1824) are not equivalent to the means; therefore, our sample is not normally distributed and the series is skewed. The 50 per cent point of a sample distribution is best described by the median for a skewed series and, since these medians are not statistically different, it can be concluded that both tags measure the same total volume.[15] The data of Schultz and associates[26] would substantiate this view, since they obtained a difference of 1.8 per cent between the T-1824 and RISA volumes. Similarly the data of Inkley and co-workers[13] revealed a difference of 5.4 per cent between T-1824 and RISA volumes.

The reproducibility is the same using the single 10-minute sample as it is using 3 samples for the calculation. The method of plotting the values for extrapolation to zero time yields an inherent difference between the 10-minute and extrapolated value; the 10-minute value is larger. The concentration of the tag at 10-minutes is always lower than the concentration projected to zero time. This method of calculation may well yield an extrapolated value which is artificially low, and there is a statistically significant difference in this direction in our figures (Table VIII), 3 per cent for RISA and 11 for T-1824. However, this difference is insignificant in practical application because the error of reproducibility is greater than this difference and the same method of calculation is ordinarily repeated in all cases, thus correcting itself. One might consider introducing a correction factor to allow for this variation.

The 10-minute sample has been found to be as satisfactory for estimation of blood volume as the more cumbersome extrapolation technique. The reproducibility (methodologic error) and actual error of the 10-minute sample method are comparable to the extrapolation method. This is a consistent finding throughout all series, including the patients with recent gastrointestinal hemorrhage. Although the clinical records of these patients with bleeding ulcer indicate that 20 per cent of them exhibited evidence of shock, the error of the single sample technique was essentially the same as with extrapolation if RISA was employed. It has been pointed out that reliance on a single sample may yield larger error in shock because of increased circulation time[11, 17, 21, 30] and vasoconstriction. Also, shock, burns, peritonitis, and similar conditions cause an increased rate of protein loss[7, 18] and dye disappearance from the circulation. In these situations, the extrapolation method perhaps should be used because it is the only reliable way of insuring against a large sampling error. Correcting for fluid shifts with a formula employing changes in protein concentration of the plasma has been suggested[23] to improve the accuracy of the 10-minute T-1824 sampling method. If protein determinations are made with the falling drop technique this may be feasible, but this method is difficult and not routinely applicable. Moreover, utilization of the extrapolation method in these cases will correct for rapid fluid shifts and yield results within the limits of accuracy possible in these abnormal states.

CONCLUSION

1. The error of the RISA method of determination of plasma volume (± 6.5 per cent) is considerably less than the error of the T-1824 method (± 17.0 per cent).

2. The principal error in the T-1824 method is a function of the variation of optical density of the plasma (± 16.2 per cent) under limitations imposed by practical application of the method.

3. The use of a single 10-minute sample for calculation results in the same error as use of the extrapolation technique.

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Pediatric Surgery

CONDUCTED BY MARK M. RAVITCH, M.D.

INTRAUTERINE INTUSSUSCEPTION AS A CAUSE OF INTESTINAL ATRESIA

A CONTRIBUTION TO THE ETIOLOGY OF INTESTINAL ATRESIAS

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THE etiology of intestinal atresias is usually explained as due to arrested development of the intestine in the solid stage during the second and third months of fetal life. This theory does not seem to offer a satisfactory explanation of all atresias.[3] We have had 3 cases of intestinal atresia operated upon at this clinic in the last 3 years, in which the cause of the atresia was an intrauterine intussusception.

CASE REPORTS

CASE 1.—L. H., the first baby, a girl, birth weight 2,050 Gm., was born of a 24-year-old mother and a 33-year-old father. The pregnancy had apparently been normal. The baby vomited intestinal contents from birth. A few apparently normal meconium stools were passed. In the roentgen examination of the intestines, at a country hospital, distended bowel loops and fluid levels were visible. The baby was sent to the Children's Clinic at the age of 6 days. The rather dehydrated baby weighed only 1,650 Gm. In the plain films of the abdomen, numerous fluid levels and small amounts of previously administered barium were visible in the stomach and small intestine. A barium enema easily passed up the narrow but otherwise apparently normal colon to the cecum, which was situated normally. From the cecum some of the contrast medium passed a few centimeters into the ileum through the ileocecal valve. At operation, through a right rectus-splitting incision, an atretic area was found 10 cm. proximal to the ileocecal valve. The ileum below the atresia was narrow, while proximally the intestine was greatly distended. About 20 cm. of the distended proximal part of the intestine was resected, with the atretic part and the tip of the distal segment. When the distal segment was opened, a polyplike prominence was seen projecting into its lumen (Fig. 1). Therefore a further portion of the distal segment was resected. An "end-to-back" anastomosis was made, after the fashion of Nixon,[16] with a single row of interrupted sutures. A proximal releasing ileostomy was performed. The first postoperative stools, through the anus, were passed on the second day, but the ileostomy was pouring out large amounts of intestinal contents. Despite 2 attempts at closure of the ileostomy, the baby succumbed to inanition and died 2 weeks postoperatively. The resected specimen showed a small bowel greatly distended proximally and ending abruptly distally. A thin, short, stringlike atretic segment connected this with the proximal end of the distal segment, in which remnants of an earlier intussusception were seen; the mucosa was partly necrotic. (Fig. 2).

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CASE 2.—R. N., a boy, birth weight 3,400 Gm., was the third child, born of a 27-year-old mother and a 26-year-old father. Three months before delivery the mother developed paralytic poliomyelitis. The baby began to vomit greenish intestinal contents at the age of one day. No flatus or meconium were passed. On admission, at the age of 2 days, the weight of the baby was 3,040 Gm. The general condition was fairly good. The abdomen was distended and soft. The scrotum was swollen and reddish and showed fluctuation. After the rectal

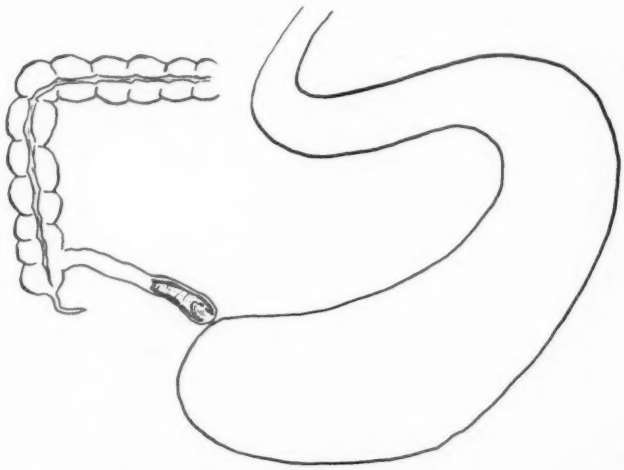

Fig. 1.—Sketch of the operative finding in Case 1. A portion of the anterior wall of the distal segment is removed to show the plug. The finding in the other 2 cases was similar, only the length of the atretic segment and the distance from the ileocecal valve varied.

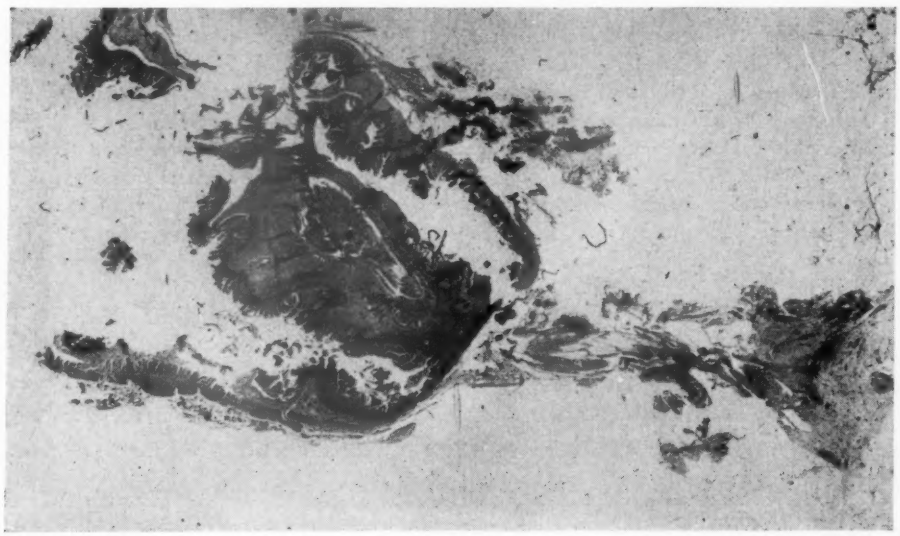

Fig. 2.—Low-power photomicrograph of the distal and atretic segment in Case 1 showing the distal segment with the plug, the short atretic segment, and the tip of the proximal segment.

examination, rather copious sticky green meconium was passed, in which Farber's test revealed some cornified epithelial cells and one lanugo hair. The plain films of the abdomen showed gas and fluid levels in the distended stomach and in some bowel loops, and, in addition, perhaps some free fluid, but no free gas, in the peritoneal cavity. A working diagnosis of meconium ileus was made, and gastric suction and fluid therapy were begun. On the subsequent days no stools were passed, and in the plain films the situation was unchanged. The

operation was performed through a right rectus-splitting incision when the baby was 4 days old. Numerous adhesions and small calcareous deposits were found on the peritoneal and intestinal surfaces, signifying meconium peritonitis. On the liver surface was a larger calcareous deposit, measuring 2.5 by 0.5 cm. A 5 cm. long, cordlike atretic segment connected the dilated upper segment with the narrow distal segment. The distal narrow ileum was covered with copious adhesions and was adherent to the cecum. In the proximal end of the distal segment an intraluminal bulb was palpated and this was assumed to be meconium. No perforation of the intestines could be found. The most enlarged distal part of the proximal segment was resected and "end-to-back" anastomosis was performed with one row of interrupted silk sutures. In the resected specimen, the atretic segment showed a minute lumen full of calcareous mass. This narrow atretic segment merged into the distal gut, in which remnants of an earlier intussusception were seen. The postoperative course was uncomplicated and the child was discharged at the age of 3 weeks.

CASE 3.—A. R., a boy, birth weight 3,700 Gm., was the fifth child of the family. The baby had vomited watery fluid since birth and several meconium stools were passed, the first one at 3 days. Because of umbilical bleeding the baby was sent to a country hospital, where the umbilical stump was sutured. In the hospital the child vomited, no more stools were passed, and, in the roentgen films of the abdomen, fluid levels could be seen. The baby was sent to this clinic at the age of 6 days with the diagnosis of intestinal stenosis. Operation was performed through a right transverse supraumbilical incision. Twenty centimeters proximal from the ileocecal valve was an atretic segment approximately 1 cm. in length and consisting only of a thin, fibrous band. Proximally the intestine was greatly distended. Distally the terminal ileum was empty and the band disappeared into the proximal end of the distal segment. When the distal segment was opened a 2.5 to 3 cm. long, tonguelike plug was seen projecting into its lumen. To the tip of this plug a hard meconium deposit was adherent. The plug was resected, with the atretic part and the distal end of the proximal segment. The nutrition of the latter seemed to be somewhat impaired. An end-to-end anastomosis was completed. In the mesentery corresponding to the atresia, there was a swelling about the size of a thumb tip, which was considered to be a lymph node. The cecum was situated normally but was rather mobile. The microscopic specimen of the plug showed that the base of it consisted of more or less normal intestinal wall. More centrally, the connective tissue increased and the tip was necrotic. The base was covered with normal intestinal mucosa, which disappeared toward the tip. The baby made an uneventful recovery and was discharged from the hospital 3 weeks after the operation.

DISCUSSION

The most prominent symptom in the 3 cases in this report was meconium or fecal vomiting since birth and abdominal distention. All the infants had passed at first what appeared to be normal meconium stools after birth. Later constipation supervened. In the plain abdominal films in all 3 cases, distended coils of intestines with fluid levels were visible. The preoperative roentgen examination with barium enema in the first case revealed a narrow but otherwise normal colon.

In all the cases, ileal atresia was found. The atretic segment was rather short, from a few millimeters to a few centimeters. In all, the cordlike atretic segment merged into the distal narrow segment. Here, a plug could be palpated, which both macroscopically and microscopically showed remnants of an earlier intussusception. In Case 3, calcified meconium was attached to the tip of this plug. In addition, a tumorlike mass was found in the mesentery of this patient. In Case 2, the cordlike atretic segment was seen to contain a calcareous mass in its lumen.

In all cases, at operation, the most dilated proximal segment, the atretic segment, and the proximal tip of the distal segment were resected. In two, an "end-to-back" anastomosis and in one an end-to-end anastomosis with a single row of interrupted sutures were performed. In Case 1, in addition, a decompressing ileostomy was performed proximal to the anastomosis. Attempts to close the ileostomy failed, and the baby died of dehydration 2 weeks postoperatively. The other 2 babies survived.

In Case 2, at operation, in addition to the atresia, numerous adhesions and calcareous deposits were found in the peritoneal cavity as a sign of meconium peritonitis. No perforation, however, could be found in the intestine. Rather similar cases have been reported by Olnick and Hatcher,[17] Lannin and associates,[12] and Nixon.[16] It seems probable that gangrenous bowel wall from intussusception was the cause of both the atresia and the perforation.

The diagnosis was delayed unusually long in two of the cases. This was mainly due to passage of fairly normal meconium stools, which, despite vomiting and abdominal distention, confused the diagnosis of atresia. In one of the present cases, Farber's test showed cornified epithelial cells and lanugo hair in the meconium. Hence, the presence of these does not seem to rule out the possibility of intestinal atresia. Nixon[16] made similar observations.

Intussusception is most frequent in infants between 4 and 10 months of age but is rare in the newborn.[7, 8, 18] Jeffrey[10] reviewed 17 cases of intussusception in the newborn from the literature and added one of his own. Louw,[14] Gross,[8] Swain and co-workers,[20] and Santulli[19] have reported additional cases. Even apparent intrauterine intussusceptions have been reported.[1, 11] In Hurwitt and Arnheim's case[9] of jejunal volvulus and meconium ileus, an early invagination of 1 cm. of the distal ileum into the cecum was found.

Recently, some reports have accumulated in which the intussusception was found in connection with intestinal atresias. Evans,[5] in an exhaustive review of 1,498 original records of reported cases of intestinal atresia, encountered 9 intussusceptions. Louw and Barnard,[15] among 22 personal cases of midgut atresias, found in one that the distal bowel segment contained remnants of intussusception.

The present 3 cases were found among 23 cases of jejunoileal atresias operated upon in this clinic during the 4-year period from 1954 through 1957. Thus, a relatively high proportion of atresias was caused by this kind of intrauterine accident.

Most of the recent monographs of pediatric surgery,[6-8] of intestinal obstruction,[4, 21] or of embryology[3] refer the etiology of intestinal atresias to arrest of development at the solid stage of the intestine between the sixth and eighth embryonic weeks. Most of the authors mentioned admit, however, that this theory does not seem to explain satisfactorily all cases of jejunoileal atresia. According to Evans,[5] this theory is not acceptable in the majority, if any, of the atresias. He believed that he had obtained definite proof that atresia is caused by some mechanical disturbance to the fetal intestine, with a frequency governed by the laws of chance. Nixon,[16] similarly, presenting strong arguments against

the old theory, suggested the more likely cause to be an accident to the fetal bowel after its formation. Louw and Barnard,[15] suggested that "vascular accidents" to the fetal intestine might cause some of the jejunoileal atresias. Experimentally, they succeeded in producing intestinal atresia after ligation of the mesentery of 2 puppies in utero. Similar results have been reported elsewhere.[2] The present cases lend support to the view that intrauterine bowel accidents occur and that they are capable of producing atresias.

The etiology of intrauterine intussusception is not known. Since the intussusception in childhood usually occurs at the time when solid food is added to the diet, a relationship to this has been suggested.[18] The solid food might alter the peristalsis.[8] During fetal life the intestinal contents consist of viscid meconium. This might stimulate the intestine to excessive peristalsis with consequent intussusception,[1] especially when the meconium is inspissated at the physiologic narrowing at the ileocecal valve.[9] Louw and Barnard[15] suggested that, after (hypothetical) intrauterine strangulation, increased peristalsis might cause the segment involved to invaginate into the distal segment. Laufman,[13] after replacement of strangulated intestinal segment in dogs, found postoperative intussusception of the involved segment into the distal bowel on many occasions. Thus, it seems probable that the viscid meconium, or some other stimulus to the fetal intestine, might cause increased peristalsis with consequent intussusception and atresia.

SUMMARY

Three cases of congenital intestinal atresia are reported, in which the cause of the atresia was intrauterine intussusception. One of the patients had meconium peritonitis. This patient, as well as one of the others, recovered after operation. Some reference is made to reports of neonatal and intrauterine intussusception. Recent reports in the literature and study of the present cases lend support to the theories that vascular accidents and accidents to the gut, including intussusception, during intrauterine life are the probable causes of congenital jejunoileal atresias.

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Reappraisal

CONDUCTED BY CLARENCE DENNIS, M.D. ASSISTED BY ALFRED HURWITZ, M.D.

THE JEJUNAL INTERPOSITION OPERATION FOR SUBSTITUTION OF THE ESOPHAGOGASTRIC SPHINCTER

PRESENT STATUS

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EXPERIMENTALLY in the dog the value of interposing a jejunal segment between the proximal esophagus and distal stomach in situations wherein the esophagogastric sphincter is excised or incised was demonstrated. From this laboratory, numerous articles have been published indicating the step-by-step evaluation of the various physiologic factors involved. In its final form, the operation consists of the interposition of an isoperistaltic segment of jejunum between the esophagus and stomach, with a bilateral vagotomy and a Finney-type pyloroplasty. The experimental results were unequivocal and the conclusions straightforward. Consequently, clinical trial seemed indicated.

On June 3, 1952, the first stage of a jejunal interposition was carried out and completed on Oct. 22, 1952. With one exception, all subsequent operations have been carried out as one-stage procedures. In 1955, the concept of cardiac "sphincter" substitution for various diseases of the esophagogastric junction was presented with the initial report of 12 cases.[1] Since that time, a total of 33 patients have been subjected to this operation for a variety of diseases in this area. The purpose of this presentation is to evaluate our experience and the results to date.

CLINICAL MATERIAL

These 33 patients were operated upon between Oct. 1, 1952, and March, 1958, a period of 5½ years. The predominant lesion treated was peptic esophagitis. In these 20 patients, varying degrees of organic stricture were common to all with associated dysphagia, substernal pain, heartburn, dietary restriction, and weight loss. Of 7 patients with symptomatic cardiospasm, four were treated primarily by excision and jejunal interposition, and in three this was a secondary procedure following the failure of previous operations. The remaining 6 patients consisted of patients with esophageal varices, secondary to extrahepatic portal bed block, lye stricture, and operatively-induced esophageal stricture. The age range was from 8 to 75 years; one-third of the patients were between 60 and 75 years of age, with a sex ratio of 2.2 males to 1 female.

RESULTS

Immediate and Late.—There have been 4 operative deaths, a mortality rate of 12 per cent. It is felt that two of these deaths were preventable. A third death resulted from poor clinical judgment. This patient was a poor candidate for this or any other operation. There have been 3 late deaths, none of which were attributable to the jejunal interposition operation. The interval from operation to death was 6 months, 12 months, and 24 months, respectively (60, 67, and 72 years of age at the time of operation). One patient has been lost to follow-up but showed an excellent result when last seen.

There has been a weight increase in approximately 70 per cent of the patients, ranging from 10 to 44 per cent over the preoperative weight. The average weight gain of these 17 patients is 14 per cent. Eight patients (32 per cent of the series) have shown an average decline in weight of 6.2 per cent. Three of the patients in the weight loss group are severe alcoholics with poor dietary habits. Usually a stationary weight level is reached and maintained within a 6-month period, after dietary readjustments have occurred and a pattern of caloric intake becomes established.

Between 3 and 9 months postoperatively many patients have experienced varying degrees of substernal and epigastric discomfort with ingestion of a normal-sized meal and therefore ate more frequently. After this period, the majority of patients eat 3 meals a day similar to other members of the family. There is no major restriction of any particular food, although 3 patients have developed a definite dislike for dairy products, particularly milk. Of the entire group, 6 patients, all operated upon over 2 years ago, have established a pattern of eating 4 to 5 times per day.

There is no dysphagia in the entire group. Seven patients, however, state that there is a delay in swallowing so that they eat more slowly. In 3 patients this is a definite though minor annoyance.

Dumping has been defined as the occurrence of sweating, unpleasant warmth, subjective flushing, weakness, palpitation, nausea, or explosive diarrhea, with the onset within 15 minutes after eating and lasting up to 45 minutes and relieved partially by lying down. Fifty-two per cent of this series experienced one or more of these symptoms in varying degrees early in the postoperative period. In only one patient was this disabling. A short period of hospitalization was required for management, and this patient is no longer incapacitated. Presently, dumping persists in 3 patients but is of no major significance. One patient, a severe chronic alcoholic, has frequent bouts of diarrhea, while 6 patients have noted occasional and transient episodes of diarrhea, possibly attributable to the vagotomy or pyloroplasty.

Three patients (12 per cent) are capable of true vomiting; that is, the regurgitation of digested or partially digested, bitter-tasting, bile-stained food. Four other patients are able to regurgitate from the esophagus and/or jejunal segment. The remaining 18 patients (48 per cent) state that they are unable to vomit. Neither clinically nor experimentally has the inability to vomit been shown to be a disadvantage.

Of 9 alcoholics in this series, six are included in the follow-up group. One patient has mild heartburn, particularly after drinking, but no esophagitis by esophagoscopy. The remaining patients are very satisfied. The longest follow-up is the first patient in this series (A. H.) who was operated upon almost 6 years ago. Despite constant alcoholic ingestion and several hospitalizations for pellagra, he is completely asymptomatic. The overindulgence in alcohol plus the associated lack of neutralizing food in the stomach constitutes a severe test indeed of the jejunal segment as well as the stomach and duodenum.

DISCUSSION

No patient, with the proper indications, has been denied surgery in an attempt to define the proper place for this procedure. While a mortality rate of 12 per cent is high, errors in judgment, surgical technique, and postoperative care have been made. However, it is in order to draw attention to the fact that one-third of the patients were in the sixth and seventh decades, and, with the exception of 3 patients, all represented treatment failures on both medical and/or surgical grounds. In one-third of the patients, the interposition operation was the second (1 patient), third (2 patients), or fourth (3 patients) major operative procedure for alleviation of the patient's disease. Consequently, the operative procedure frequently was complicated by previous surgery.

In all symptomatic patients prior to surgery, there has not been a single failure of the operation. All surviving patients have been relieved of their original complaints.

SUMMARY

To date there has been no evidence of recurrence of the disease for which the patient has been operated upon. As previously noted, the patient has traded certain minor symptoms as a consequence of the operative procedure, a not infrequent situation following many different operations. However, there is no other group of patients more grateful and satisfied with the over-all result. While the operation in our hands has had a mortality rate in excess of what one might hope, this is not an uncommon experience with any new major operative procedure.

The operator has several choices in the surgical management of the disease entities for which the jejunal interposition has been utilized. Other procedures may carry a lesser risk but at the same time frequently are associated with an imperfect result or frank failure. In fact, in this series, many cases represent failures of other operative procedures. Thus, whether one utilizes the jejunal interposition operation or a lesser procedure remains, in part, a matter of philosophy.

In truth, the diseases for which this operation has been undertaken result in prolonged, severe disability and frequently death of the patient over a period of time if untreated, or if treated improperly. Our philosophy has been, and continues to be, that of accepting a somewhat higher operative risk

in this group of patients in order to obtain a cure of the disease. It is hoped that continued experience with the procedure will result in a reduced risk to subsequent patients.

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In Memoriam

Arthur Wilburn Allen

1887-1958

Surgery lost one of its most ardent and loyal supporters in the death of Arthur Wilburn Allen on March 19, 1958. Dr. Allen had been a member of the Editorial Board of Surgery since its inception. He had contributed to it not only in the form of scientific papers, but also by his wise counsel that was always of great service to the Editorial Board. Dr. Allen was born in McKinney, Kentucky, on Nov. 30, 1887. He received an A.B. degree from Georgetown (Kentucky) College in 1909 and was given an honorary Sc.D. degree in 1943. He attended The Johns Hopkins University School of Medicine, from which he received an M.D. degree in 1913. Following graduation, he went to the Massachusetts General Hospital in Boston, where he received his early surgical training under the late George Washington Brewster. In 1936, he was appointed Chief of the East Surgical Service at the Massachusetts General Hospital, retaining this position until his retirement in 1948, when he was named Consultant in Surgery and later, Honorary Surgeon. In 1953, he was appointed a Trustee of the Hospital by gubernatorial order.

During World War I, Dr. Allen served in France as a Captain in the Medical Corps and during World War II was a member of the Subcommittee on Vascular Injuries for the National Research Council. He also served on the Commission on Physical Rehabilitation under the Federal Security Agency. From 1936 to 1948, he served as Lecturer in Surgery at the Harvard Medical School and did a tremendous amount of clinical work, particularly on abdominal surgery.

Dr. Allen was greatly respected by the medical profession and received every honor the profession could bestow upon him. He was President of the Boston Surgical Society in 1942, the Society of Vascular Surgery in 1948, the Massachusetts Medical Society in 1949, and the Pan-Pacific Surgical Society from 1954 to 1958. Unfortunately, he was unable to preside at the meeting in 1958 because of his terminal illness. He was Chairman of the United States Committee of the International Society of Surgery in 1950. Dr. Allen was President of the American College of Surgeons in 1947-1948, a member of the Board of Regents from 1936 to 1951, and Chairman from 1949 to 1951.

Dr. Allen was Director of the Massachusetts Blue Cross Plan from 1949 to 1958 and the Blue Shield Plan from 1945 to 1953. He was a Trustee of the Governor Dummer Academy in South Byfield.

He was a member of the Society of Clinical Surgery, the Surgical Research Society, the American Surgical Association, the Southern Surgical Association, the New England Surgical Society, and the Society for Vascular Surgery. He received many honorary memberships, being an honorary Fellow of the Royal College of Surgeons and the Royal Society of Medicine of England. He was also a Fellow of the Royal College of Surgeons of Edinburgh and a member of the French Academy of Surgery.

Dr. Allen was a physician's doctor, which is the highest tribute that can be paid to anyone practicing medicine. Because of his tremendous experience, his uncanny judgment, and his dexterous skill, his services were sought by many individuals, including members of the medical profession. He was an extremely kind person, had a rare sense of humor, and had a faculty of expressing himself in the most lucid and pleasing manner. Because of these qualities, he was an extremely popular speaker at medical meetings and, when he spoke, the hall was always filled, because everyone knew he would learn something really worth while and something that could be relied upon. He was the epitome of integrity.

Dr. Allen was extremely fortunate in having married a childhood sweetheart, Vida Weddle, who was a great help and inspiration to him and whose stimulation and encouragement played a great part in his success. The Allens had one son, Arthur Wilburn, Jr., and four grandchildren.

In Jimmie's death, the world lost a great physician and a real scientist. Those of us who knew him lost a true and loyal friend. The Editorial Board of SURGERY will greatly miss him.

—ALTON OCHSNER

Book Reviews

CONDUCTED BY J. GARROTT ALLEN, M. D.

Surgery of the Chest. Johnson, Julian, and Kirby, Charles K. Ed. 2. Chicago, 1958, Year-book Publishers, Inc. Price $9.75.

Published in 1958, the second edition of *Surgery of the Chest* is one of the series of handbooks of operative surgery. As the preface states, the book is primarily an atlas of thoracic surgical operations. While differential diagnosis, etiology, life history, and pathology are not discussed, the text is by no means merely a catalog of operations. Generous sections of the book are devoted to discussions of normal and pathologic surgical anatomy and physiology, pre- and postoperative care and the special problems arising during major thoracic procedures. The diagnostic techniques used to evaluate chest lesions are briefly described in general terms. The arrangement of the material in the text is systematic and logical while the style is concise and to the point, although readability is not sacrificed to brevity. A bibliography has been purposely omitted.

Surgery of the Chest is divided into thirteen chapters containing descriptions of almost every surgical procedure of the chest wall, lungs, heart, esophagus, diaphragm, and mediastinum. An almost identical format is used for each of the chapters. In each section a brief introduction to the subject precedes a discussion of the indications for surgery, the positioning of the patient, the incisions used, and the operative care of the patient. The technique of surgery, illustrated on facing pages, is then detailed in semi-outline form followed by a discussion of postoperative care and complications. The chapter dealing with the surgery of the heart and great vessels includes an up-to-date section on the problems and procedures of hypothermia and cardiac bypass. The volume is amply illustrated with clearly executed and carefully labeled drawings adding greatly to the understanding of the text.

Surgery of the Chest is a compact manual that provides a great deal of information useful to students of general surgery interested in the technique of thoracic surgery. It would be a valuable addition to the library of the student at any level.

—Edward A. Stemmer

The Rudolph Matas History of Medicine in Louisiana. John Duffy. Volume I. Baton Rouge, La., 1958, The Louisiana State University Press. Pp. 522. Price $10.00.

Because Dr. Matas spent a good deal of his lifetime collecting material for the *History of Medicine in Louisiana,* the first volume by John Duffy is indeed a masterpiece. Although the monograph is concerned with the history of medicine in Louisiana, it gives a good insight into the early colonial days in the South and portrays a great deal about the life of the early settlers. Volume I is divided into three parts: Part I, Louisiana under France, 1699-1768; Part II, Louisiana under Spain, 1769-1803; and Part III, The Transitional Period, 1804-1825.

Included in the first part is a chapter on Indian medicine, one on early hospitals of the period, and another on local botanical remedies that the pioneers found when the area

was settled. The influence of the introduction of slaves into the South and the effect upon the health in this area are described in detail. One cannot help being impressed by the primitive methods that were employed and the great difficulty that was encountered in combating disease, particularly smallpox, yellow fever, and the diarrheas. The work is authoritative and the references are very complete. Every student of history should have this book in his library, because it is a classic as far as medical history is concerned.

—Alton Ochsner

Introduction to Chest Surgery. Geoffrey Flavell. London, 1957, Oxford University Press. Pp. 354. Price $7.50.

This book consists of three parts: the first and major section deals with the surgery of the lungs, pleura, and thoracic cavity; the other two parts deal with surgery of the esophagus, heart, and great vessels.

As the author has stated in the preface, this book is intended for the student. Its purpose has been achieved to a large extent, for it is succinct in presentation, easily read with clear understanding, and serves as an excellent introduction to thoracic surgery for the beginner in this field. It is fairly comprehensive and covers the basic principles and methods of treatment well. These are supplemented with well-chosen case histories and illustrations.

It is understandable that the size of the book prevents extensive coverage of each subject. However, the discussion of the basic physiology and anatomy of the lungs is sketchy and somewhat inadequate, and the section on congenital heart lesions does not include open heart techniques.

Nonetheless, this book should prove valuable in assisting the student to understand the diagnostic problems that may be encountered and their management.

—A. Al-Shamma

Textbook of Gynecology. John I. Brewer, Baltimore, 1958, Williams & Wilkins Company. Price $15.00.

This is the second edition of an excellent gynecologic text. The material of the previous edition has been expanded, pertinent new information has been added, and the basic concepts of current gynecologic theory and practice have been accurately and concisely set forth.

The general plan of this book is admirable. Part One is clinically oriented. Gynecologic entities are presented from the standpoint of their signs and symptoms in relationship to the three major periods of a woman's life. Part Two is devoted to the traditional textbook discussion of these entities.

Numerous well-chosen illustrations and references enhance the value of this book, which has been expertly adapted to the needs of the undergraduate student, for whom it was primarily written.

Charles P. McCartney

Abdominal Operations by the Vaginal Route. Paul Warner and Julius Sederi. Translated by L. M. Szamek. Philadelphia and New York, 1958, J. B. Lippincott Company. Price $9.00.

This work was written by two Viennese gynecologists for the purpose of presenting a comprehensive description of the techniques utilized in the performance of pelvic surgery by the vaginal route. They have succeeded in their objective, with the result that this book, which is unique in current medical literature, fills the long-existing need for a compact surgical manual dealing with this aspect of pelvic surgery.

The vaginal procedures which the authors describe include vaginal hysterectomy and removal of the adnexae, total extirpation of the fibromyomatous uterus by morcellation, myomectomy, cysto-oophorectomy, salpingectomy for tubal pregnancy, tubal sterilization, and antefixation of the uterus. Some of the authors' indications for these vaginal procedures are at variance with current American gynecologic opinion, which considers the puncture and removal of any cystic ovarian neoplasm by the vaginal route to be inadvisable. Likewise, the surgical treatment of endometrial carcinoma by the vaginal route is generally not regarded as the treatment of choice in this country. On the other hand, when an easily accessible, uncomplicated tubal pregnancy is discovered at colpotomy, its removal by the vaginal route, as advocated by the authors, is a logical procedure.

The text is clear and concise. The surgical procedures are adequately illustrated by black and white drawings, and pre- and postoperative care are thoroughly discussed. The value of this work is enhanced by the authors' references to their extensive experience with these vaginal procedures.

This authoritative, compact, comprehensive atlas of vaginal surgical technique is a valuable contribution to current medical literature.

Charles P. McCartney

INDEX TO VOLUME 44

AUTHOR INDEX*

A

ABBOTT, JACK P., COOLEY, DENTON A., DEBAKEY, MICHAEL E., AND RAGLAND, JAMES E. Storage of blood for open heart operation, 698

ABBOTT, WM. E. (*See* Krieger et al.), 138

ACKERMAN, LAUREN V. (*See* Hershey et al.), 1008

ACTIS-DATO, A. (*See* Dogliotti et al.), 706

ADAMS, JESSE E. (*See* Owens et al.), 240

ADLER, RICHARD H., FIRME, CONSTANTE N., AND LANIGAN, JOHN M. A valve mechanism to prevent gastroesophageal reflux and esophagitis, 63

—, LIBASSI, PAUL J., AND STOLL, HENRY C. Comparative resistance of the esophagus to acid and pepsin, 795

ADRIANI, JOHN. (*See* Trotti and Adriani), 515

AIKMAN, WILLIAM O. (*See* Hershey et al.), 1008

ALBERT, H. M., ATIK, M., AND FOWLER, R. Production and release of pulmonary stenosis in dogs, 904

ANTHONY, J. E. (*See* Rendleman et al.), 640

ARTZ, CURTIS P., STANLEY, THOMAS V., JR., EURE, WILLIAM R., LANGFORD, HERBERT G., AND SNAVELY, JOHN R. Inflow and outflow changes in ammonia concentrations of liver, muscle, and brain, 22

ATIK, M. (*See* Albert et al.), 904

AXELROD, A. E. (*See* Fisher et al.), 149

B

BACANER, MARVIN B. (*See* Connolly et al.), 255

BACON, HARRY E. (*See* McGregor and Bacon), 828

BAHNSON, HENRY T. (*See* Brockman et al.), 910

—. (*See* Spencer et al.), 109

BAKER, MILDRED. (*See* Flom et al.), 356

BAKER, NORMAN H., KIRKLIN, JOHN W., GRINDLAY, JOHN H., AND EDWARDS, JESSE E. Use of autografts to bridge defects in arteries of coronary size, 548

BANNER, ROBERT L. (*See* Pack and Banner), 1024

BARET, A. C., PATTERSON, L. T., MACKIE, J. A., AND BLAKEMORE, W. S. The effect of cabbage factor on the peptic ulcer of Mann-Williamson dogs, 817

BERNARD, CHRISTIAAN N. (*See* Snyder et al.), 1083

BARNES, WILLIAM H., ELLIS, F. HENRY, JR., GRINDLAY, JOHN H., AND EDWARDS, JESSE E. Experimental production of pulmonary hypertension, 361

BARNETT, WILLIAM O., AND DOYLE, RICHARD S. The effects of neomycin upon the toxicity of peritoneal fluid resulting from strangulation obstruction, 442

BASCOM, G. S. (*See* Eiseman et al.), 854

BASCOM, JOHN. (*See* Hitchcock et al.), 492

BEAL, JOHN M. (*See* Cornell et al.), 125

BEATTIE, E. J., JR. (*See* Rendleman et al.), 640

BENJAMIN, ROBERT B. (*See* Flom et al.), 356

BERNARDO, JOHN R., SODERBERG, CLARENCE H., AND MIGLIACCIO, ANTHONY V. Gastric ulcer, 804

BERNE, CLARENCE J., AND MIKKELSEN, WILLIAM P. Management of perforated peptic ulcer, 591

BERNSTEIN, EUGENE F., GREENSPAN, RICHARD H., AND LOKEN, MERLE K. Intravenous abdominal aortography, 529

BEST, RICHARD J. (*See* Gianelli et al.), 378

BINKLEY, FREDERICK M. (*See* Clausen et al.), 735

BLAKEMORE, W. S. (*See* Baret et al.), 817

BLALOCK, ALFRED. (*See* Sabiston and Blalock), 406

BOBA, ANTONIO. (*See* Powers et al.), 53

BODON, GEORGE R., AND LAPUZ, BIENVENIDO. Acute small bowel obstruction with sigmoid diverticulitis and its management, 631

BOOHER, ROBERT J. (*See* Bowden and Booher), 963

BOSSENMAIER, IRENE. (*See* Snyder et al.), 1083

BOWDEN, LEMUEL, AND BOOHER, ROBERT J. The principles and technique of resection of soft parts for sarcoma, 963

*July, pp. 1-264; August, pp. 265-434; September, pp. 435-612; October, pp. 613-784; November, pp. 785-962; December, pp. 963-1138.

BOYCE, FREDERICK FITZHERBERT. Regional enteritis in a large general hospital, 834

BRADHAM, R. RANDOLPH. Imperforate anus, 578

BRITT, CLARENCE I., KOONS, RONALD B., AND WATMAN, ROBERT N. A method of identification of intestinal bleeding experimentally produced in dogs, 844

BROCKMAN, STANLEY K., WEBB, ROSCOE C., JR., AND BAHNSON, HENRY T. Monopolar ventricular stimulation for the control of acute surgically produced heart block, 910

BROOKS, A. J. (*See* Rendleman et al.), 640

BROWDER, E. JEFFERSON. (*See* Cook et al.), 338

BROWN, IVAN W., JR., SMITH, WIRT W., AND EMMONS, W. O. An efficient blood heat exchanger for use with extracorporeal circulation, 372

BRUNS, DAVID L. (*See* Connolly et al.), 255

BUENGER, R. E. (*See* Rendleman et al.), 640

BURKE, JOHN F. (*See* Welch and Burke), 943

BURROUGHS, JOHN T. (*See* Longmire et al.), 572

BURTON, CLAUD C. Current concepts of the anatomic, clinical, and reparative features of femoral hernia, 877

BUTCHER, HARVEY R., JR. A simple technique for endarterectomy, 984

BUXTON, R. W. (*See* Reynolds et al.), 33

C

CALDWELL, ELBERT H. Anastomosis of the branches of the facial and spinal accessory nerves for facial paralysis, 978

CALMAN, CARL, HERSHEY, FALLS B., SKAGGS, JEROME O., AND SPENCER, ANDREW. Serum lactic dehydrogenase in the diagnosis of the acute surgical abdomen, 43

CALVANESE, NICHOLAS. (*See* Fisher et al.), 149

CARLSON, ROBERT I. (*See* Foster and Carlson), 1034

CARREÑO, M. PÉREZ. (*See* de Bellard and Carreño), 627

CASSIE, GORDON F. (*See* Couch et al.), 666

CATCHPOLE, B. N., AND CURRAN, R. C. A new type of arterial prosthesis, 994

CLAUSEN, EDWIN G., JAKE, ROBERT J., AND BINKLEY, FREDERICK M. Contralateral inguinal exploration of unilateral hernia in infants and children, 735

CLOWES, GEORGE H. A., JR., NEVILLE, WM. E., SABGA, GABRIEL, AND SHIBOTA, YUKATA. The relationship of oxygen consumption, perfusion rate, and temperature to the acidosis associated with cardiopulmonary circulatory bypass, 220

CODINGTON, J. B. (*See* Reynolds et al.), 33

COFFEY, R. J. (*See* Donahue et al.), 1070

COLE, WARREN H. (*See* Jackson et al.), 1092

COLEY, BRADLEY L., AND HIGINBOTHAM, NORMAN. Indications for hemipelvectomy, 766

COLLINS, MAE. (*See* Hitchcock et al.), 492

CONNELL, JAMES F., JR., AND ROUSSELOT, LOUIS M. Preliminary studies on a new intestinal bactericide—Soframycin, 447

CONNOLLY, JOHN E., BACANER, MARVIN B., BRUNS, DAVID L., LOWENSTEIN, JEROLD, AND STORLI, EDGAR. Mechanical support of the circulation in acute heart failure, 255

COOK, ALBERT W., FREUND, H. ROBERT, AND BROWDER, E. JEFFERSON. Venous patterns following occlusion of the jugular system as demonstrated by jugular venography, 338

COOLEY, DENTON A. (*See* Abbott et al.), 698

COPENHAVER, W. M. (*See* Reemtsma et al.), 99

CORNELL, GEORGE N., GILDER, HELENA, FILIPPONE, AMES, FULLER, F. W., AND BEAL, JOHN M. Changes in body compartments following operation, 125

COUCH, NATHAN P., CASSIE, GORDON F., AND MURRAY, JOSEPH E. Survival of the excised dog kidney perfused in a pump-oxygenator system. I. Circulatory changes in the hypothermic preparation, 666

CRAIGHEAD, CLAUDE C., AND STRUG, LAWRENCE H. Diaphragmatic deficiency in the retrocostoxiphoid area, 1062

CREECH, OSCAR, JR. (*See* Reemtsma et al.), 99

CURRAN, R. C. (*See* Catchpole and Curran), 994

CUTAIT, DAHER E. (*See* Montenegro and Cutait), 785

D

DAVIS, C., JR. (*See* Rendleman et al.), 640

DAWSON, ROYCE E. (*See* Owens et al.), 240

DEBAKEY, MICHAEL E. (*See* Abbott et al.), 698

DE BELLARD, E. P., AND CARREÑO, M. PÉREZ. Granulomatous tumors and neoplasms of the colon and anorectal zone in Venezuela, 627

DE CHOLNOKY, TIBOR. Mastectomies with simultaneous reconstruction of breasts, 689

DERRICK, JOHN R., AND LOGAN, W. D. Mesenteric arterial insufficiency, 823

DE TAKATS, GEZA. (*See* Villavicencio and de Takats), 312

DEWEESE, JAMES A. Functional popliteal phlebography in the patient with a complicated varicose vein problem, 390

DeWeese, M. S. (*See* Feller and DeWeese), 540
Dogliotti, A. M., Actis-Dato, A., and Gentilli, R. Digital and instrumental commissurotomy in mitral stenosis, 706
Donahue, J. K., Houck, J. C., and Coffey, R. J. Serum desoxyribonuclease activity and pancreatic damage, 1070
Doyle, Richard S. (*See* Barnett and Doyle), 442

E

Edwards, Jesse E. (*See* Baker et al.), 548
—. (*See* Barnes et al.), 361
Eiseman, B., Silen, W., Bascom, G. S., and Kauvar, A. J. Fecal enema as an adjunct in the treatment of pseudomembranous enterocolitis, 854
Ellis, F. Henry, Jr. (*See* Barnes et al.), 361
—. (*See* Kuykendall et al.), 718
Emmons, W. O. (*See* Brown et al.), 372
Enerson, Daniel M. (*See* Mayo and Enerson), 91
Eure, William R. (*See* Artz et al.), 22

F

Feller, Irving, and DeWeese, M. S. The use of stored cutaneous autografts in wound treatment, 540
Ferguson, D. J. (*See* Thorngate and Ferguson), 619
Filippone, Ames. (*See* Cornell et al.), 125
Firme, Constante N. (*See* Adler et al.), 63
Fisher, Bernard, Axelrod, A. E., Fisher, E. R., Lee, S. H., and Calvanese, Nicholas. The favorable effect of pyridoxine deficiency on skin homograft survival, 149
Fisher, E. R. (*See* Fisher et al.), 149
Flom, Robert S., Benjamin, Robert B., Turbak, Charles E., MacLean, Lloyd D., and Lewis, F. John. Atherosclerotic changes in grafts of the thoracic aorta, 356
Foster, John H., and Carlson, Robert I. Gastrojejunal ulcer presenting as a mass in the abdominal wall, 1034
Fowler, R. (*See* Albert et al.), 904
Freund, H. Robert. (*See* Cook et al.), 338
Frieden, Julian H., and Shulman, Alexander G. The risk of section of the sphincter of Oddi, 860
Fuller, F. W. (*See* Cornell et al.), 125

G

Gentilli, R. (*See* Dogliotti et al.), 706
Gianelli, Stanley, Jr., Robinson, James H., Best, Richard J., and Kirby, Charles K. Hemodynamic mechanisms which automatically maintain a relatively constant blood volume during cardiopulmonary bypass, 378
Gibbon, John H., Jr. (*See* Schechter et al.), 892
Gibson, James. (*See* Localio et al.), 625
Gilder, Helena. (*See* Cornell et al.), 125
Glas, Wayne W. (*See* Lui et al.), 295
Goldsmith, N. A., and Ransom, H. K. Choledochostomy, 868
Greenspan, Richard H. (*See* Bernstein et al.), 529
Gregg, R. O. (*See* Rustad et al.), 726
Grindlay, John H. (*See* Baker et al.), 548
—. (*See* Barnes et al.), 361
—. (*See* Kuykendall et al.), 718
Grossi, Carlo. (*See* Miller et al.), 402

H

Hagerty, Robert F., and Jeffords, J. Vernon. Dressings: fabric versus plastic, 556
Hallenbeck, George A. Gastric resection with end-to-end cholecystoduodenostomy in a case of duodenal ulcer with obstruction to common bile duct, 850
Haller, J. Alex, Jr. Second shunting operations for pulmonary stenosis with cyanosis following failure of original systemic-pulmonary anastomoses, 919
Harder, Helen. (*See* Hitchcock et al.), 492
Hardin, Creighton A., Werder, Alvar A., and Russell, Garth. Induced lymphosarcoma resulting from the transplantation of skin grafts from animals treated with 20-methylcholanthrene, 176
Hardin, Robert. (*See* Su et al.), 1079
Harper, Harold A. (*See* Mawdsley et al.), 287
—. (*See* Najarian et al.), 11
Haynes, Lewis L. (*See* Thorbjarnarson and Haynes), 585
Helfman, Lillian. (*See* Hitchcock et al.), 492
Hendrick, James W. Results of treatment of cystic disease of the breast, 457
Herrington, J. Lynwood, Jr. The Billroth I and Billroth II reconstructions, 1040
—. The pyloric antrum—the relative extent of distal gastrectomy necessary to insure its complete extirpation (Edit.), 775
Herron, Paul W., Jesseph, John E., and Merendino, K. Alvin. The effects of arterenol on blood pressure and venous return during extracorporeal circulation, 398
Hershey, Falls B. (*See* Calman et al.), 43
—, Aikman, William O., Ackerman, Lauren V., and Stamp, Warren G. Pathologic and radiographic studies of amputated extremities, 1008
Higinbotham, Norman. (*See* Coley and Higinbotham), 766

HINSHAW, J. RAYMOND, AND PEARSE, HERMAN E. The feasibility of investigating the effect of local medication on burn healing, 886
HITCHCOCK, CLAUDE R., HARDER, HELEN, PANUSKA, MARGARET, COLLINS, MAE, HELFMAN, LILLIAN, MIGAKI, HOYA, AND BASCOM, JOHN. Control of surgical infections at the Minneapolis General Hospital, 492
—. (*See* Kiser and Hitchcock), 936
HOLDEN, WM. D. (*See* Krieger et al.), 138
HORN, ROBERT C., JR. (*See* Moran and Horn), 683
HOUCK, J. C. (*See* Donahue et al.), 1070
HOWARD, JOHN M. (*See* Jordan and Howard), 303
HUSNI, ELIAS A. (*See* Simeone et al.), 168
HUTCHINSON, WILLIAM B., AND KIRILUK, LAWRENCE B. Parotid tumors, 483

I

IMAMOGLU, KAMIL. (*See* Wangensteen et al.), 265

J

JACKSON, BENJAMIN B. Observations on intraperitoneal adhesions, 507
JACKSON, KENNETH, MCGREW, ELIZABETH, AND COLE, WARREN H. Prophylactic treatment of the Murphy Sturm rat lymphosarcoma with nitrogen mustard, 1092
JAKE, ROBERT J. (*See* Clausen et al.), 735
JEFFORDS, J. VERNON. (*See* Hagerty and Jeffords), 556
JENSON, CONRAD B. (*See* Wangensteen et al.), 265
JESSEPH, JOHN E. (*See* Herron et al.), 398
JEZIORO, Z., AND KUS, H. Experiences with the retrosternal esophageal replacement employing jejunum or ileum, 275
JORDAN, GEORGE L., JR., AND HOWARD, JOHN M. Caudal pancreatojejunostomy in the management of chronic relapsing pancreatitis, 303

K

KAJIKURI, HISASHI. (*See* Moore et al.), 345
KARLAN, MITCHELL. (*See* Traphagen and Karlan), 644
KARLSON, KARL E. (*See* Senn and Karlson), 1095
KAUVAR, A. J. (*See* Eiseman et al.), 854
KAY, EARLE B., NOGUEIRA, CID, AND ZIMMERMAN, H. A. Direct vision correction of mitral insufficiency, 325
KEELER, WILLIAM H. (*See* Lui et al.), 295
KING, HAROLD. (*See* Su et al.), 1079
KIRBY, CHARLES K. (*See* Gianelli et al.), 378
—. (*See* McCaughan et al.), 210
KIRILUK, LAWRENCE B. (*See* Hutchinson and Kiriluk), 483
KIRKLIN, JOHN W. (*See* Baker et al.), 548
KISER, JOSEPH C., AND HITCHCOCK, CLAUDE R. Comparative studies with a new plastic surgical mask, 936
KLAUSNER, CLAIRE. (*See* Richards and Klausner), 181
KOLETSKY, SIMON. (*See* Stueber et al.), 77
KONDO, TATSUHEI. (*See* Moore and Kondo), 199
KOONS, RONALD B. (*See* Britt et al.), 844
KOVACS, STEVEN. (*See* Stueber et al.), 77
KRIEGER, HARVEY, ABBOTT, WM. E., LEVEY, STANLEY, AND HOLDEN, WM. D. Reevaluation of the role of the adrenal and other factors in the metabolic response to surgery, 138
KUS, H. (*See* Jezioro and Kus), 275
KUYKENDALL, SAM J., ELLIS, F. HENRY, JR., AND GRINDLAY, JOHN H. Surgical correction of chronic mitral insufficiency in dogs, 718

L

LANCE, EDWARD M. (*See* Owens et al.), 240
LANG, STANLEY. (*See* Sisson et al.), 613
LANGFORD, HERBERT G. (*See* Artz et al.), 22
LANIGAN, JOHN M. (*See* Adler et al.), 63
LAPUZ, BIENVENIDO. (*See* Bodon and Lapuz), 631
LARGO, DONALD J. (*See* Lui et al.), 295
LEE, S. H. (*See* Fisher et al.), 149
LESLIE, MALCOLM B. (*See* Schenk et al.), 333
LEVEY, STANLEY. (*See* Krieger et al.), 138
LEWIN, ELIS. (*See* Miller et al.), 402
LEWIS, F. JOHN. (*See* Flom et al.), 356
—. Hemorrhoidectomy—need for a sound appraisal (Edit.), 431
—. (*See* Reeves and Lewis), 84
LIBASSI, PAUL J. (*See* Adler et al.), 795
LILLEHEI, C. WALTON. (*See* Snyder et al.), 1083
LOCALIO, S. ARTHUR, LOWMAN, EDWARD W., AND GIBSON, JAMES. Wound healing in the paraplegic patient, 625
LOGAN, W. D. (*See* Derrick and Logan), 823
LOKEN, MERLE K. (*See* Bernstein et al.), 529
LONGMIRE, WILLIAM P., JR., BURROUGHS, JOHN T., AND MALONEY, JAMES V., JR. Total anomalous pulmonary venous connection, 572
LOWENSTEIN, JEROLD M. (*See* Connolly et al.), 255
LOWMAN, EDWARD W. (*See* Localio et al.), 625
LUI, ALFRED H. F., GLAS, WAYNE W., KEELER, WILLIAM H., AND LARGO, DONALD J. Paradoxical motion of the abdominal wall in rupture of the diaphragm, 295

M

McCaughan, James S., Jr., McMichael, Harrison, Schuder, John C., and Kirby, Charles K. The use of a totally occlusive pump as a flowmeter with observations on hemolysis caused by occlusive and nonocclusive pumps and other pump-oxygenator components, 210

McCaughan, John J., Jr. Surgical exposure of the distal popliteal artery, 536

McCorkle, H. J. (*See* Mawdsley et al.), 287

—. (*See* Najarian et al.), 11

McGregor, Robert A., and Bacon, Harry E. Multiple cancers in colon surgery, 828

McGrew, Elizabeth. (*See* Jackson et al.), 1092

Mackie, J. A. (*See* Baret et al.), 817

MacLean, Lloyd D. (*See* Flom et al.), 356

McMichael, Harrison. (*See* McCaughan et al.), 210

Majnarich, George, and Malament, Maxwell. Urinary tract metastases by cancers of large bowel, 520

Malament, Maxwell. (*See* Majnarich and Malament), 520

Maloney, James V., Jr. (*See* Longmire et al.), 572

Mawdsley, Dean L., Silen, William, Weirich, William L., Harper, Harold A., and McCorkle, H. J. An experimental study of iron absorption following total gastrectomy, 287

Mayo, Henry W., Jr., and Enerson, Daniel M. Endocrine influences of the pancreas on gastric secretion. I. The effects of glucagon and alloxan on Heidenhain pouch secretion, 91

Merendino, K. Alvin. (*See* Herron et al.), 398

—, and Thomas, George I. The jejunal interposition operation for substitution of the esophagogastric sphincter, 1112

Michele, Arthur A. The flip sign in sciatic nerve tension, 940

Migaki, Hoya. (*See* Hitchcock et al.), 492

Migliaccio, Anthony V. (*See* Bernardo et al.), 804

Mikkelsen, William P. (*See* Berne and Mikkelsen), 591

Miller, Theodore R., Grossi, Carlo, and Lewin, Elis. Parasitization of isolated small bowel loops in dogs, 402

Montenegro, Edwin Benedito, and Cutait, Daher E. Construction of a new esophagus by means of the transverse colon and its application for caustic atresia, carcinoma, and varices of the esophagus, 785

Moore, Francis D. The university in American surgery, 1

Moore, George E., and Kondo, Tatsuhei. Study of adjuvant cancer chemotherapy by model experiments, 199

Moore, Richard O. (*See* Smythe and Moore), 561

Moore, Thomas C. Lobectomy for postpneumonic lung abscess in infancy and childhood, 741

—, and Riberi, Angelo. Superior vena caval replacement. III. Successful use of fresh autogenous aorta, 898

—, —, Kajikuri, Hisashi, and Shumacker, Harris B., Jr. Use of impedance plethysmography in evaluation of peripheral vascular response to arteriography, 345

Moran, John J., and Horn, Robert C., Jr. Carcinoma of sweat gland origin, 683

Morton, John J. Surgical philosophy, 927

Moschel, Daniel M., Walske, Benedict R., and Neumayer, Francis. A new technique of pyloroplasty, 813

Murray, Joseph E. (*See* Couch et al.), 666

N

Najarian, John S., Harper, Harold A., and McCorkle, H. J. Amino acid therapy of ammonia intoxication, 11

Nakamura, Yoshihiko. (*See* Powers et al.), 53

Nealon, Thomas F., Jr. (*See* Schechter et al.), 892

Neill, Catherine A. (*See* Spencer et al.), 109

Neumayer, Francis. (*See* Moschel et al.), 813

Neville, Wm. E. (*See* Clowes et al.), 220

Nogueira, Cid. (*See* Kay et al.), 325

O

Ochsner, Alton. In memoriam to Arthur Wilburn Allen, 1116

Owens, Guy, Adams, Jesse E., Dawson, Royce E., Lance, Edward M., Sawyers, John L., and Scott, H. William, Jr. Observed central nervous system responses during experimental employment of various pump-oxygenators, 240

P

Pack, George T., and Banner, Robert L. The late development of gastric cancer after gastroenterostomy and gastrectomy for peptic ulcer and benign pyloric stenosis, 1024

Panuska, Margaret. (*See* Hitchcock et al.), 492

Pareira, Morton D. (*See* Pipes and Pareira), 636

—. (*See* Sisson et al.), 613

PARKKULAINEN, K. V. Intrauterine intussusception as a cause of intestinal atresia, 1106
PATE, JAMES W. Urokon portograms in dogs, 570
PATTERSON, L. T. (*See* Baret et al.), 817
PEARSE, HERMAN E. (*See* Hinshaw and Pearse), 886
PELTIER, LEONARD F. Joseph François Malgaigne and Malgaigne's fracture, 777
PERSKY, LESTER. (*See* Stueber et al.), 77
PHELAN, JOHN T. A new method of artery graft anastomosis, 990
PIPES, KEITH E., AND PAREIRA, MORTON D. Duodenal obstruction appearing after palliative biliary diversion for pancreatic carcinoma, 636
PLZAK, LOUIS, PRICE, LINDA, AND WOODWARD, EDWARD R. The effect of complete exclusion of the stomach on fat and nitrogen absorption, 299
PORTIN, BERTRAM A. (*See* Schenk et al.), 333
POWERS, SAMUEL R., JR., SCHAFFER, CHARLES, BOBA, ANTONIO, AND NAKAMURA, YOSHIHIKO. Physical and biologic factors in impedance plethysmography, 53
PRICE, LINDA. (*See* Plzak et al.), 299
PRIOR, J. T. (*See* Rustad et al.), 726

R

RAGLAND, JAMES E. (*See* Abbott et al.), 698
RANDALL, H. T. (*See* Rush and Randall), 655
RANSOM, H. K. (*See* Goldsmith and Ransom), 868
RAVITCH, MARK M., AND SNYDER, GILBERT B. Congenital cystic dilatation of the common bile duct, 752
REEMTSMA, KEITH, COPENHAVER, W. M., AND CREECH, OSCAR, JR. The cardiac conduction system in congenital anomalies of the heart, 99
REEVES, MELVIN M., AND LEWIS, F. JOHN. Total body cooling in critically ill febrile patients, 84
RENDLEMAN, D. F., ANTHONY, J. E., DAVIS, C., JR., BUENGER, R. E., BROOKS, A. J., AND BEATTIE, E. J., JR. Reflux pressure studies on the ileocecal valve of dogs and humans, 640
REYNOLDS, B. L., CODINGTON, J. B., AND BUXTON, R. W. Wound healing: a study of the response of injured tissues to the coenzyme adenosine 5-monophosphate, 33
RIBERI, ANGELO. (*See* Moore and Riberi), 898
—. (*See* Moore et al.), 345
RICHARDS, VICTOR, AND KLAUSNER, CLAIRE. The heterologous transplantation of human cancer in untreated Swiss-Webster mice, 181
ROBINSON, JAMES H. (*See* Gianelli et al.), 378
ROE, BENSON B. A simple device to facilitate coronary artery perfusion, 554
ROOT, HARLAN D. (*See* Wangensteen et al.), 265
ROUSSELOT, LOUIS M. (*See* Connell and Rousselot), 447
RUSH, B. F., JR., AND RANDALL, H. T. Postsurgical anuria: an experimental study of fluid and electrolyte changes, 655
RUSSELL, GARTH. (*See* Hardin et al.), 176
RUSTAD, HERMAN I., GREGG, R. O., AND PRIOR, J. T. The effect of hypercholesterolemia upon aortic homografts and Teflon-nylon prostheses in the rabbit, 726

S

SABGA, GABRIEL. (*See* Clowes et al.), 220
SABISTON, DAVID C., JR., AND BLALOCK, ALFRED. Physiologic and anatomic determinants of coronary blood flow and their relationship to myocardial revascularization, 406
SALMON, PETER A. (*See* Wangensteen et al.), 265
SAWYERS, JOHN L. (*See* Owens et al.), 240
SCANLON, EDWARD F. (*See* Staley and Scanlon), 646
SCHAFFER, CHARLES. (*See* Powers et al.), 53
SCHECHTER, DAVID C., NEALON, THOMAS F., JR., AND GIBBON, JOHN H., JR. A simple extracorporeal device for reducing elevated blood ammonia levels, 892
SCHENK, WORTHINGTON G., JR., PORTIN, BERTRAM A., AND LESLIE, MALCOLM B. The electronic measurement of cardiac output, 333
SCHNEEWIND, JOHN H. Intensive preoperative nutritional therapy, 424
SCHUDER, JOHN C. (*See* McCaughan et al.), 210
SCHWARTZ, AARON M. The historical development of methods of hemostasis, 604
SCOTT, H. WILLIAM, JR. (*See* Owens et al.), 240
SENN, LAVONNE Y., AND KARLSON, KARL E. Methodologic and actual error of plasma volume determination, 1095
SERKES, KENNETH. (*See* Sisson et al.), 613
SHIBOTA, YUKATA. (*See* Clowes et al.), 220
SHULMAN, ALEXANDER G. (*See* Frieden and Shulman), 860
SHUMACKER, HARRIS B., JR. (*See* Moore et al.), 345
SICHER, NELLE. (*See* Sisson et al.), 613
SILEN, W. (*See* Eiseman et al.), 854
—. (*See* Mawdsley et al.), 287
SIMEONE, F. A., HUSNI, ELIAS A., AND WEIDNER, MICHAEL G., JR. The effect of l-norepinephrine upon the myocardial oxygen tension and survival in acute hemorrhagic hypotension, 168

SISSON, RICHARD, LANG, STANLEY, SERKES, KENNETH, AND PAREIRA, MORTON D. Comparison of wound healing in various nutritional deficiency states, 613
SKAGGS, JEROME O. (*See* Calman et al.), 43
SMITH, WIRT W. (*See* Brown et al.), 372
SMYTHE, RICHARD L., AND MOORE, RICHARD O. A study of possible humoral factors in liver regeneration in the rat, 561
SNAVELY, JOHN R. (*See* Artz et al.), 22
SNYDER, DAVID D., BARNARD, CHRISTIAAN N., VARCO, RICHARD L., AND LILLEHEI, C. WALTON. Serum transaminase patterns following intracardiac surgery, 1083
SNYDER, GILBERT B. (*See* Ravitch and Snyder), 752
SODERBERG, CLARENCE H. (*See* Bernardo et al.), 804
SPENCER, ANDREW. (*See* Calman et al.), 43
SPENCER, FRANK C., NEILL, CATHERINE A., AND BAHNSON, HENRY T. The treatment of congenital aortic stenosis with valvotomy during cardiopulmonary bypass, 109
STALEY, CHARLES J., AND SCANLON, EDWARD F. Urinary diversion, 646
STAMP, WARREN G. (*See* Hershey et al.), 1008
STANLEY, THOMAS V., JR. (*See* Artz et al.), 22
STOLL, HENRY C. (*See* Adler et al.), 795
STORLI, EDGAR. (*See* Connolly et al.), 255
STRODE, J. E. Subphrenic abscess, 1054
STRUG, LAWRENCE H. (*See* Craighead and Strug), 1062
STUEBER, PAUL, KOVACS, STEVEN, KOLETSKY, SIMON, AND PERSKY, LESTER. Regional renal hypothermia, 77
SU, CHIEN SHENG, HARDIN, ROBERT, AND KING, HAROLD. The use of hypothermia with cardiopulmonary bypass for open heart surgery, 1079
SWYRYD, ELIZABETH. (*See* Flom et al.), 356

T

TAYLOR, FREDERIC W., AND VELLIOS, FRANK. Failure to prove identity of tumor cells in the peripheral blood, 453
THOMAS, GEORGE I. (*See* Merendino and Thomas), 1112
THORBJARNARSON, BJORN, AND HAYNES, LEWIS L. Duplication of the stomach, 585
THORNGATE, S., AND FERGUSON, D. J. Effect of tension on healing of aponeurotic wounds, 619
TRAPHAGEN, DONALD W., AND KARLAN, MITCHELL. Fluorescein string test for localization of upper gastrointestinal hemorrhage, 644
TROTTI, WILLIAM, AND ADRIANI, JOHN. A comparison of the antisecretory and vagolytic effects of the belladonna alkaloids and certain synthetic parasympatholytic drugs, 515
TURBAK, CHARLES E. (*See* Flom et al.), 356
TURELL, ROBERT. A rebuttal to "hemorrhoidectomy—need for a sound reappraisal" (Edit.), 959

V

VARCO, RICHARD L. (*See* Snyder et al.), 1083
VELLIOS, FRANK. (*See* Taylor and Vellios), 453
VILLAVICENCIO, J. LEONEL, AND DE TAKATS, GEZA. Mast cell activity under various forms of stress, 312

W

WALSKE, BENEDICT, R. (*See* Moschel et al.), 813
WANGENSTEEN, OWEN H., ROOT, HARLAN D., JENSON, CONRAD B., IMAMOGLU, KAMIL, AND SALMON, PETER A. Depression of gastric secretion and digestion by gastric hypothermia: its clinical use in massive hematemesis, 265
WARREN, RICHARD, AND WYSOCKI, ALICE. Assay of heparin in blood: a critique, 435
WATMAN, ROBERT N. (*See* Britt et al.), 844
WEBB, ROSCOE C., JR. (*See* Brockman et al.), 910
WEIDNER, MICHAEL G., JR. (*See* Simeone et al.), 168
WEIRICH, WILLIAM L. (*See* Mawdsley et al.), 287
WELCH, CLAUDE E., AND BURKE, JOHN F. An appraisal of the treatment of gastric ulcer, 943
WERDER, ALVAR A. (*See* Hardin et al.), 176
WOODWARD, EDWARD R. (*See* Plzak et al.), 299
WYSOCKI, ALICE. (*See* Warren and Wysocki), 435

Z

ZIMMERMAN, H. A. (*See* Kay et al.), 325

SUBJECT INDEX*

A

Abdominal aortography, intravenous (Bernstein et al.), 529
operations by the vaginal route (B. rev.), 1119
surgery, acute, serum lactic dehyrogenase in diagnosis of (Calman et al.), 43
wall, gastrojejunal ulcer presenting as mass in (Foster and Carlson), 1034
paradoxical motion of, in rupture of diaphragm (Lui et al.), 295
Abscess, lung, postpneumonic, lobectomy for, in infancy and childhood (Moore), 741
subphrenic (Strode), 1054
Acid and pepsin, comparative resistance of esophagus to (Adler et al.), 795
Acidosis associated with cardiopulmonary bypass, relationship of oxygen consumption, perfusion rate, and temperature to (Clowes et al.), 220
ACTH, effect of, on normal and heparinized mast cells (Villavicencio and de Takats), 312
Adenosine 5-monophosphate, response of injured tissues to, in wound healing (Reynolds et al.), 33
Address, presidential, of Society of University Surgeons (Moore), 1
Adhesions, intraperitoneal, observations of (Jackson), 507
Adjuvant cancer chemotherapy, study of, by model experiments (Moore and Kondo), 199
Adrenal and other factors in metabolic response to surgery (Krieger et al.), 138
Alkaloids, belladonna, and certain parasympatholytic drugs, antisecretory and vagolytic effects of (Trotti and Adriani), 515
Allen, Arthur Wilburn, in memoriam, 1116
Alloxan and glucagon in Heidenhain pouch secretion; endocrine influences of pancreas on gastric secretion (Mayo and Enerson), 91
Amino acid therapy of ammonia intoxication (Najarian et al.), 11
Ammonia concentrations of liver, muscle, and brain, inflow and outflow changes in (Artz et al.), 22
intoxication, amino acid therapy of (Najarian et al.), 11
levels, blood, elevated, simple extracorporeal device for reducing (Schechter et al.), 892
Amputated extremities, pathologic and radiographic studies of (Hershey et al.), 1008
Anastomoses, systemic-pulmonary, failure of, second shunting operations for pulmonary stenosis with cyanosis following (Haller), 919
Anastomosis, artery graft, new method of (Phelan), 990
of branches of facial and spinal accessory nerves for facial paralysis (Caldwell), 978
Anemia, hypochromic, following total gastrectomy (Mawdsley et al.), 287
Anomalous pulmonary venous connection, total (Longmire et al.), 572
Anorectal zone and colon, granulomatous tumors and neoplasms of, in Venezuela (de Bellard and Carreño), 627
Antisecretory and vagolytic effects of belladonna alkaloids and certain synthetic parasympatholytic drugs (Trotti and Adriani), 515
Antrum, pyloric, relative extent of distal gastrectomy necessary to insure complete extirpation of (Edit.), 775
Anuria, postsurgical, experimental study of fluid and electrolyte changes in (Rush and Randall), 655
Anus, imperforate (Bradham), 578
Aorta, autogenous, fresh, successful use of, in superior vena caval replacement (Moore and Riberi), 898
Aortic grafts, thoracic, atherosclerotic changes in (Flom et al.), 356
homografts and Teflon-nylon prostheses in rabbit, effect of hypercholesterolemia on (Rustad et al.), 726
stenosis, congenital, treatment of, with valvotomy during cardiopulmonary bypass (Spencer et al.), 109
Aortography, abdominal, intravenous (Bernstein et al.), 529
Aponeurotic wounds, effect of tension on healing of (Thorngate and Ferguson), 619
Arginine in ammonia intoxication (Najarian et al.), 11
Arterenol in blood pressure and venous return during extracorporeal circulation (Herron et al.), 398
Arterial hypertension, pulmonary, experimental production of (Barnes et al.), 361

*July, pp. 1-264; August, pp. 265-434; September, pp. 435-612; October, pp. 613-784; November, pp. 785-962; December, pp. 963-1138.

Arterial—Cont'd
insufficiency, mesenteric (Derrick and Logan), 823
prosthesis, new nylon (Catchpole and Curran), 994
Arteries of coronary size, autografts to bridge defects in (Baker et al.), 548
Arteriography, peripheral vascular response to, impedance plethysmography in evaluation of (Moore et al.), 345
Artery graft anastomosis, new method of (Phelan), 990
perfusion, coronary, transaortic, needle to facilitate (Roe), 554
popliteal, distal, surgical exposure of (McCaughan), 536
stenosis, pulmonary, production and release of, in dogs (Albert et al.), 904
Assay of heparin in blood (Warren and Wysocki), 435
Atherosclerotic changes in grafts of thoracic aorta (Flom et al.), 356
Atresia, caustic, carcinoma, and varices of esophagus, construction of new esophagus by means of transverse colon and its application for (Montenegro and Cutait), 785
intestinal, intrauterine intussusception as cause of (Parkkulainen), 1106
Autogenous aorta, fresh, successful use of, in superior vena caval replacement (Moore and Riberi), 898
arterial grafts of small diameter, function and survival of, following end-to-end anastomosis (Baker et al.), 548
Autografts to bridge defects in arteries of coronary size (Baker et al.), 548
cutaneous, stored, in wound treatment (Feller and DeWeese), 540

B

Belladonna alkaloids and certain synthetic parasympatholytic drugs, antisecretory and vagolytic effects of (Trotti and Adriani), 515
Bile duct, common, congenital cystic dilatation of (Ravitch and Snyder), 752
obstruction to, gastric resection with end-to-end cholecystoduodenostomy in duodenal ulcer with (Hallenbeck), 850
Biliary diversion, palliative, for pancreatic carcinoma, duodenal obstruction appearing after (Pipes and Pareira), 636
Billroth I and Billroth II reconstructions (Herrington), 1040
Biologic and physical factors in impedance plethysmography (Powers et al.), 53
Bleeding, intestinal, method of identification of, experimentally produced in dogs (Britt et al.), 844
Blood ammonia levels, elevated, simple extracorporeal device for reducing (Schechter et al.), 892
assay of heparin in (Warren and Wysocki), 435
flow, coronary, physiologic and anatomic determinants of, and their relationship to myocardial revascularization (Sabiston and Blalock), 406
heat exchanger for use in extracorporeal circulation (Brown et al.), 372
peripheral, failure to prove identity of tumor cells in (Taylor and Vellios), 543
pressure and venous return, arterenol in, during extracorporeal circulation (Herron et al.), 398
storage of, for open heart operations (Abbott et al.), 698
volume, constant, hemodynamic mechanisms which maintain, during cardiopulmonary bypass (Gianelli et al.), 378
Book reviews, 433, 611, 784, 1118
Bowel, large, cancers of, urinary tract metastases by (Majnarich and Malament), 520
loops, small, isolated, in dogs, parasitization of (Miller et al.), 402
obstruction, acute small, with sigmoid diverticulitis and its management (Bodon and Lapuz), 631
Brain, liver, and muscle, ammonia concentrations of, inflow and outflow changes in (Artz et al.), 22
Breast, cystic disease of, results of treatment of (Hendrick), 457
Breasts, simultaneous reconstruction of, mastectomies with (de Cholnoky), 689
Burn healing, effect of local medication on (Hinshaw and Pearse), 886
Bypass, cardiopulmonary, electroencephalographic observations during (Owens et al.), 240
hemodynamic mechanisms which maintain constant blood volume during (Gianelli et al.), 378
treatment of congenital aortic stenosis with valvotomy during (Spencer et al.), 109
use of hypothermia with, for open heart surgery (Su et al.), 1079
circulatory, cardiopulmonary, acidosis associated with, relationship of oxygen consumption, perfusion rate, and temperature to (Clowes et al.), 220
venous-to-arterial, femoral, as support of circulation in acute heart failure (Connolly et al.), 255

C

Cabbage factor, effect of, on peptic ulcer of Mann-Williamson dogs (Baret et al.), 817
Calendar of surgical meetings, 264, 434, 612, 765, 962

Cancer chemotherapy, adjuvant, study of, by model experiments (Moore and Kondo), 199
gastric, after gastroenterostomy and gastrectomy for peptic ulcer and benign pyloric stenosis (Pack and Banner), 1024
human, heterologous transplantation of, in untreated Swiss-Webster mice (Richards and Klausner), 181
Cancers of large bowel, urinary tract metastases by (Majnarich and Malament), 520
multiple, in colon surgery (McGregor and Bacon), 828
Carcinoma, caustic atresia, and varices of esophagus, construction of new esophagus by means of transverse colon and its application for (Montenegro and Cutait), 785
pancreatic, palliative biliary diversion for, duodenal obstruction appearing after (Pipes and Pareira), 636
of sweat gland origin (Moran and Horn), 683
Carcinomas, multiple of rectum and colon (McGregor and Bacon) 828
Cardiac conduction system in congenital anomalies of heart (Reemtsma et al.), 99
output, electronic measurement of (Schenk et al.), 333
Cardiopulmonary bypass, electroencephalographic observations during (Owens et al.), 240
hemodynamic mechanisms which maintain constant blood volume during (Gianelli et al.), 378
treatment of congenital aortic stenosis with valvotomy during (Spencer et al.), 109
use of hypothermia with, for open heart surgery (Su et al.), 1079
circulatory bypass, acidosis associated with, relationship of oxygen consumption, perfusion rate, and temperature to (Clowes et al.), 220
Caudal pancreatojejunostomy in chronic relapsing pancreatitis (Jordan and Howard), 303
Caustic atresia, carcinoma, and varices of esophagus, construction of new esophagus by means of transverse colon and its application for (Montenegro and Cutait), 785
Central nervous system responses during experimental employment of various pump-oxygenators (Owens et al.), 240
Chemotherapy, cancer, adjuvant, study of, by model experiments (Moore and Kondo), 199
Cholecystoduodenostomy, end-to-end, gastric resection with, in duodenal ulcer with obstruction to common bile duct (Hallenbeck), 850
Choledochostomy (Goldsmith and Ransom), 868
Circulation, extracorporeal, arterenol in blood pressure and venous return during (Herron et al.), 398
blood heat exchanger for use with (Brown et al.), 372
support of, femoral venous-to-arterial bypass as, in acute heart failure (Connolly et al.), 255
Circulatory bypass, cardiopulmonary, acidosis associated with, relationship of oxygen consumption, perfusion rate, and temperature to (Clowes et al.), 220
changes in hypothermic preparation of excised dog kidney perfused in pump-oxygenator system (Couch et al.), 666
Coenzyme adenosine 5-monophosphate response of injured tissues to, in wound healing (Reynolds et al.), 33
Colon and anorectal zone, granulomatous tumors and neoplasms of, in Venezuela (de Bellard and Carreño), 627
and rectum, multiple carcinomas of (McGregor and Bacon), 828
transverse, construction of new esophagus by means of, and its application for caustic atresia, carcinoma, and varices of esophagus (Montenegro and Cutait), 785
Commissurotomy, digital and instrumental, in mitral stenosis (Dogliotti et al.), 706
Common bile duct, congenital cystic dilatation of (Ravitch and Snyder), 752
obstruction to, gastric resection with end-to-end cholecystoduodenostomy in duodenal ulcer with (Hallenbeck), 850
Compleat pediatrician, the (B. rev.), 611
Conduction system, cardiac, in congenital anomalies of heart (Reemtsma et al.), 99
Congenital anomalies of heart, cardiac conduction system in (Reemtsma et al.), 99
aortic stenosis, treatment of, with valvotomy during cardiopulmonary bypass (Spencer et al.), 109
cystic dilatation of common bile duct (Ravitch and Snyder), 752
Contralateral inguinal exploration of unilateral hernia in infants and children (Clausen et al.), 735
Control of surgical infections at Minneapolis General Hospital (Hitchcock et al.), 492
Coronary artery perfusion, needle to facilitate (Roe), 554
blood flow, physiologic and anatomic determinants of, and their relationship to myocardial revascularization (Sabiston and Blalock), 406
size, arteries of, autografts to bridge defects in (Baker et al.), 548
Cryptorchism (B. rev.), 611

Cutaneous autografts, stored, in wound treatment (Feller and DeWesse), 540
Cyanosis, pulmonary stenosis with, following failure of systemic-pulmonary anastomoses, second shunting operations for (Haller), 919
Cystic dilatation, congenital, of common bile duct (Ravitch and Snyder), 752
disease of breast, results of treatment of (Hendrick), 457

D

Desoxypyridoxine in skin homograft survival (Fisher et al.), 149
Desoxyribonuclease, serum, activity and pancreatic damage (Donahue et al.), 1070
Diaphragm, rupture of, paradoxical motion of abdominal wall in (Lui et al.), 295
Diaphragmatic deficiency in retrocostoxiphoid area (Craighead and Strug), 1062
Digestion and gastric secretion, depression of, by gastric hypothermia in massive hematemesis (Wangensteen et al.), 265
Digital and instrumental commissurotomy in mitral stenosis (Dogliotti et al.), 706
Dilatation, cystic, congenital, of common bile duct (Ravitch and Snyder), 752
Direct vision correction of mitral insufficiency (Kay et al.), 325
Diversion, biliary, palliative, for pancreatic carcinoma, duodenal obstruction appearing after (Pipes and Pareira), 636
urinary; metabolic alterations associated with use of isolated ileal segments (Staley and Scanlon), 646
Diverticulitis, sigmoid, acute small bowel obstruction with, and its management (Bodon and Lapuz), 631
DNA activity and pancreatic activity (Donahue et al.), 1070
Dressings, comparison of fine mesh rayon with perforated Mylar (Hagerty and Jeffords), 556
Duodenal obstruction appearing after palliative biliary diversion for pancreatic carcinoma (Pipes and Pareira), 636
ulcer with obstruction to common bile duct, gastric resection with end-to-end cholecystoduodenostomy in (Hallenbeck), 850
Duplication of stomach (Thorbjarnarson and Haynes), 585

E

Electroencephalographic observations during cardiopulmonary bypass (Owens et al.), 240
Electrolyte and fluid changes, experimental study of, in postsurgical anuria (Rush and Randall), 655
Electromagnetic flowmeter in measurement of cardiac output (Schenk et al.), 333
Endarterectomy, simple technique for (Butcher), 984
Endocrine influences of pancreas on gastric secretion; glucagon and alloxan in Heidenhain pouch secretion (Mayo and Enerson), 91
Enema, fecal, as adjunct in treatment of pseudomembranous enterocolitis (Eiseman et al.), 854
Enteritis, regional, in large general hospital (Boyce), 834
Enterocolitis, pseudomembranous, fecal enema as adjunct in treatment of (Eiseman et al.), 854
Error, methodologic and actual, of plasma volume determination (Senn and Karlson), 1095
Esophageal replacement, retrosternal, employing jejunum or ileum (Jezioro and Kus), 275
Esophagitis and gastroesophageal reflux, valve mechanism to prevent (Adler et al.), 63
Esophagogastric sphincter, jejunal interposition operation for substitution of (Merendino and Thomas), 1112
Esophagogastrostomy, high, relationship of comparative resistance of esophagus to acid and pepsin to esophagitis following (Adler et al.), 795
Esophagus, comparative resistance of, to acid and pepsin (Adler et al.), 795
new, construction of, by means of transverse colon and its application for caustic atresia, carcinoma, and varices of esophagus (Montenegro and Cutait), 785
Extracorporeal circulation, arterenol in blood pressure and venous return during (Herron et al.), 398
blood heat exchanger for use with (Brown et al.), 372
device for reducing elevated blood ammonia levels (Schechter et al.), 892

F

Fabric dressings versus plastic dressings (Hagerty and Jeffords), 556
Facial paralysis, anastomosis of branches of facial and spinal accessory nerves for (Caldwell), 978
Fat changes, body, following operation (Cornell et al.), 125
and nitrogen absorption, complete exclusion of stomach in (Plzak et al.), 299
Febrile patients, critically ill, total body cooling in (Reeves and Lewis), 84
Fecal enema as adjunct in treatment of pseudomembranous enterocolitis (Eiseman et al.), 854

Femoral hernia, current concepts of anatomic, clinical, and reparative features of (Burton), 877
venous-to-arterial bypass as support of circulation in acute heart failure (Connolly et al.), 255
Flip sign in sciatic nerve tension (Michele), 940
Flowmeter, electromagnetic, in measurement of cardiac output (Schenk et al.), 333
use of totally occlusive pump as, with observations on hemolysis caused by occlusive and nonocclusive pumps and other pump-oxygenator components (McCaughan et al.), 210
Fluid and electrolyte changes, experimental study of, in postsurgical anuria (Rush and Randall), 655
peritoneal, toxicity of, resulting from strangulation obstruction, neomycin in (Barnett and Doyle), 442
Fluorescein string test for localization of upper gastrointestinal hemorrhage (Traphagen and Karlan), 644
Fracture, Malgaigne's, and Joseph François Malgaigne (Peltier), 777
Framycetin sulfate (Soframycin), a new intestinal bactericide, preliminary studies on (Connell and Rousselot), 447
Furacin Soluble Dressing compared with perforated Mylar dressing (Hagerty and Jeffords), 556

G

Gastrectomy, distal, relative extent of, necessary to insure complete extirpation of pyloric antrum (Edit.), 775
and gastroenterostomy for peptic ulcer and benign pyloric stenosis, gastric cancer after (Pack and Banner), 1024
total, experimental study of iron absorption following (Mawdsley et al.), 287
Gastric cancer after gastroenterostomy and gastrectomy for peptic ulcer and benign pyloric stenosis (Pack and Banner), 1024
duplications (Thorbjarnarson and Haynes), 585
hypothermia, depression of gastric secretion and digestion by, in massive hematemesis (Wangensteen et al.), 265
resection with end-to-end cholecystoduodenostomy in duodenal ulcer with obstruction to common bile duct (Hallenbeck), 850
secretion and digestion, depression of, by gastric hypothermia in massive hematemesis (Wangensteen et al.), 265
Gastric—Cont'd
endocrine influences of pancreas on; glucagon and alloxan in Heidenhain pouch secretion (Mayo and Enerson), 91
ulcer (Bernardo et al.), 804
appraisal of treatment of (Welch and Burke), 943
Gastroduodenal disease, Billroth I and Billroth II reconstructions in treatment of (Herrington), 1040
perforation due to peptic ulcer, management of (Berne and Mikkelsen), 591
Gastroenterostomy and gastrectomy for peptic ulcer and benign pyloric stenosis, gastric cancer after (Pack and Banner), 1024
Gastroesophageal reflux and esophagitis, valve mechanism to prevent (Adler et al.), 63
Gastrointestinal bleeding, method of identification of, experimentally produced in dogs (Britt et al.), 844
hemorrhage, upper, fluorescein string test for localization of (Traphagen and Karlan), 644
Gastrojejunal ulcer presenting as mass in abdominal wall (Foster and Carlson), 1034
Glucagon and alloxan in Heidenhain pouch secretion; endocrine influences of pancreas on gastric secretion (Mayo and Enerson), 91
Graft anastomosis, artery, new method of (Phelan), 990
Grafts, aortic, thoracic, atherosclerotic changes in (Flom et al.), 356
skin, transplantation of, from animals treated with 20-methylcholanthrene, induced lymphosarcoma from (Hardin et al.), 176
Granulomatous tumors and neoplasms of colon and anorectal zone in Venezuela (de Bellard and Carreño), 627

H

Healing of aponeurotic wounds, effect of tension on (Thorngate and Ferguson), 619
burn, effect of local medication on (Hinshaw and Pearse), 886
wound, comparison of, in various nutritional deficiency states (Sisson et al.), 613
in paraplegic patient (Localio et al.), 625
Heart block, acute surgically produced, monopolar ventricular stimulation for control of (Brockman et al.), 910
congenital anomalies of, cardiac conduction system in (Reemtsma et al.), 99
failure, acute, femoral venous-to-arterial bypass as support of circulation in (Connolly et al.), 255

Heart—Cont'd
open, surgery, use of hypothermia with cardiopulmonary bypass for (Su et al.), 1079
storage of blood for (Abbott et al.), 698
Heat exchanger, blood, for use with extracorporeal circulation (Brown et al.), 372
Heidenhain pouch secretion, alloxan and glucagon in; endocrine influences of pancreas on gastric secretion (Mayo and Enerson), 91
Hematemesis, massive, depression of gastric secretion and digestion by gastric hypothermia in (Wangensteen et al.), 265
Hemipelvectomy, indication for (Coley and Higinbotham), 766
Hemodynamic mechanisms which maintain constant blood volume during cardiopulmonary bypass (Gianelli et al.), 378
Hemolysis caused by occlusive and nonocclusive pumps and other pump-oxygenator components, use of totally occlusive pump as flowmeter with observations on (McCaughan et al.), 210
Hemorrhage, upper gastrointestinal, fluorescein string test for localization of (Traphagen and Karlan), 644
Hemorrhagic hypotension, acute, l-norepinephrine in myocardial oxygen tension and survival in (Simeone et al.), 168
Hemorrhoidectomy—need for appraisal (Edit.), 431
need for sound reappraisal," rebuttal to (Edit.), 959
Hemostasis, historical development of methods of (Schwartz), 604
Heparin, assay of, in blood (Warren and Wysocki), 435
histologic effect of preloading mast cells with (Villavicencio and de Takats), 312
Hernia, diaphragmatic, defects in retrocostoxiphoid area in treatment of (Craighead and Strug), 1062
femoral, current concepts of anatomic, clinical, and reparative features of (Burton), 877
unilateral, in infants and children, contralateral inguinal exploration of (Clausen et al.), 735
Heterologous transplantation of human cancer in untreated Swiss-Webster mice (Richards and Klausner), 181
Historical development of methods of hemostasis (Schwartz), 604
Homograft survival, skin, pyridoxine deficiency in (Fisher et al.), 149
Homografts, aortic, and Teflon-nylon prostheses in rabbit, effect of hypercholesterolemia on (Rustad et al.), 726
Humoral factors, possible, in liver regeneration of rat (Smythe and Moore), 561
Hypercholesterolemia, effect of, on aortic homografts and Teflon-nylon prostheses in rabbit (Rustad et al.), 726
Hypertension, pulmonary, experimental production of (Barnes et al.), 361
Hypochromic anemia following total gastrectomy (Mawdsley et al.), 287
Hypotension, hemorrhagic, acute, l-norepinephrine in myocardial oxygen tension and survival in (Simeone et al.), 168
Hypothermia in critically ill febrile patients (Reeves and Lewis), 84
gastric, depression of gastric secretion and digestion by, in massive hematemesis (Wangensteen et al.), 265
renal, regional (Stueber et al.), 77
use of, with cardiopulmonary bypass for open heart surgery (Su et al.), 1079
Hypothermic preparation, circulatory changes in, of excised dog kidney perfused in pump-oxygenator system (Couch et al.), 666

I

Ileal segments, isolated, use of, in urinary diversion, metabolic alterations associated with (Staley and Scanlon), 646
Ileocecal valve, reflux pressure studies on, of dogs and humans (Rendleman et al.), 640
Ileum or jejunum, retrosternal esophageal replacement employing (Jezioro and Kus), 275
Impedance plethysmography in evaluation of peripheral vascular response to arteriography (Moore et al.), 345
physical and biologic factors in (Powers et al.), 53
Imperforate anus (Bradham), 578
Infections, surgical, control of, at Minneapolis General Hospital (Hitchcock et al.), 492
Inflow and outflow changes in ammonia concentrations of liver, muscle, and brain (Artz et al.), 22
Inguinal exploration, contralateral, of unilateral hernia in infants and children (Clausen et al.), 735
Inguinofemoral hernia, current concepts of anatomic, clinical, and reparative features of (Burton), 877
Instrumental and digital commissurotomy in mitral stenosis (Dogliotti et al.), 706
Insufficiency, arterial, mesenteric (Derrick and Logan), 823
mitral, chronic, correction of, in dogs (Kuykendall et al.), 718
Intestinal atresia, intrauterine intussusception as cause of (Parkkulainen), 1106

Intestinal—Cont'd
bactericide (Soframycin), preliminary studies on (Connell and Rousselot), 447
bleeding, method of identification of, experimentally produced in dogs (Britt et al.), 844
Intoxication, ammonia, amino acid therapy of (Najarian et al.), 11
Intracardiac surgery, serum transaminase patterns following (Snyder et al.), 1083
Intraperitoneal adhesions, observation of (Jackson), 507
Intrauterine intussusception as cause of intestinal atresia (Parkkulainen), 1106
Intravenous abdominal aortography (Bernstein et al.), 529
Introduction to chest surgery (B. rev.), 1119
Intussusception, intrauterine, as cause of intestinal atresia (Parkkulainen), 1106
Iron absorption following total gastrectomy, experimental study of (Mawdsley et al.), 287
Ischemia, lethal, regional renal hypothermia as protection against (Stueber et al.), 77

J

Jejunal interposition operation for substitution of esophagogastric sphincter (Merendino and Thomas), 1112
Jejunum or ileum, retrosternal esophageal replacement employing (Jezioro and Kuz), 275
Jugular venography, venous patterns following occlusion of jugular system demonstrated by (Cook et al.), 338

K

Kidney, dog, excised, survival of, perfused in pump-oxygenator system; circulatory changes in hypothermic preparation (Couch et al.), 666

L

Lactic dehydrogenase, serum, in diagnosis of acute surgical abdomen (Calman et al.), 43
Legs, amputated, pathologic and radiographic studies of (Hershey et al.), 1008
Liver, muscle, and brain, ammonia concentrations of, outflow and inflow changes in (Artz et al.), 22
regeneration in rat, possible humoral factors in (Smythe and Moore), 561
Lobectomy for postpneumonic lung abscess in infancy and childhood (Moore), 741
Lung abscess, postpneumonic, lobectomy for, in infancy and childhood (Moore), 741
Lymphosarcoma, induced, from transplantation of skin grafts from animals treated with 20-methylcholanthrene (Hardin et al.), 176
Murphy Sturm rat, nitrogen mustard in treatment of (Jackson et al.), 1092

M

Malgaigne, Joseph François, and Malgaigne's fracture (Peltier), 777
Mask, surgical, plastic, comparative studies with (Kiser and Hitchcock), 936
Mast cell activity under various forms of stress (Villavicencio and de Takats), 312
Mastectomies with simultaneous reconstruction of breasts (de Cholnoky), 689
Measurement, electronic, of cardiac output (Schenk et al.), 333
Medication, local, effect of, on burn healing (Hinshaw and Pearse), 886
Meeting, Society of University Surgeons, review of (Richards), 263
Meetings, surgical, calendar of, 264, 434, 612, 765, 962
Mesenteric arterial insufficiency (Derrick and Logan), 823
Metabolic alterations associated with use of isolated ileal segments in urinary diversion (Staley and Scanlon), 646
reactions of transaminase and synthesis of urea in ammonia intoxication (Najarian et al.), 11
response to surgery, adrenal and other factors in (Krieger et al.), 138
Metastases, urinary tract, by cancers of large bowel (Majnarich and Malament), 520
Metastatic carcinoma of sweat gland origin (Moran and Horn), 683
20-Methylcholanthrene, induced lymphosarcoma from transplantation of skin grafts from animals treated with (Hardin et al.), 176
Mitral insufficiency, direct vision correction of (Kay et al.), 325
in dogs, surgical correction of (Kuykendall et al.), 718
stenosis, digital and instrumental commissurotomy in (Dogliotti et al.), 706
Monopolar ventricular stimulation for control of acute surgically produced heart block (Brockman et al.), 910
Muscle, liver, and brain, ammonia concentrations of, inflow and outflow changes in (Artz et al.), 22
Mylar dressings, perforated, comparison with fine mesh rayon dressings (Hagerty and Jeffords), 556
Myocardial oxygen tension and survival in acute hemorrhagic hypotension, l-norepinephrine in (Simeone et al.), 168
revascularization, physiologic and anatomic determinants of coronary blood flow and their relationship to (Sabiston and Blalock), 406

N

National Clinical Adjuvant Chemotherapy Program, comments on, in study of adjuvant cancer chemotherapy (Moore and Kondo), 199
Needle, perfusion, to facilitate transaortic coronary artery perfusion (Roe), 554
Neomycin in toxicity of peritoneal fluid resulting from strangulation obstruction (Barnett and Doyle), 442
Neoplasms and granulomatous tumors of colon and anorectal zone in Venezuela (de Bellard and Carreño), 627
Nerve tension, sciatic, flip sign in (Michele), 940
Nerves, facial and spinal accessory, anastomosis of branches of, for facial paralysis (Caldwell), 978
Nervous system responses, central, during experimental employment of various pump-oxygenators (Owens et al.), 240
Newburgh's formula for changes in body fat, modification of, in postoperative patients (Cornell et al.), 125
Nitrogen and fat absorption, complete exclusion of stomach in (Plzak et al.), 299
  mustard in treatment of Murphy Sturm rat lymphosarcoma (Jackson et al.), 1092
Nonocclusive and occlusive pumps and other pump-oxygenator components, use of totally occlusive pump as flowmeter with observations on hemolysis caused by (McCaughan et al.), 210
l-Norepinephrine in myocardial oxygen tension and survival in acute hemorrhagic hypotension (Simeone et al.), 168
Nutritional deficiency states, various, comparison of wound healing in (Sisson et al.), 613
  therapy, preoperative, intensive (Schneewind), 424
Nylon arterial prosthesis, new type of (Catchpole and Curran), 994
  -Teflon prostheses and aortic homografts in rabbit, effect of hypercholesterolemia on (Rustad et al.), 726

O

Obstruction, acute small bowel, with sigmoid diverticulitis and its management (Bodon and Lapuz), 631
  to common bile duct, gastric resection with end-to-end cholecystoduodenostomy in duodenal ulcer with (Hallenbeck), 850
  duodenal, appearing after palliative biliary diversion for pancreatic carcinoma (Pipes and Pareira), 636
  strangulation, neomycin in toxicity of peritoneal fluid resulting from (Barnett and Doyle), 442
Occlusion of jugular system, venous patterns following, demonstrated by jugular venography (Cook et al.), 338
Occlusive pump, totally, use of, as flowmeter with observations on hemolysis caused by occlusive and nonocclusive pumps and other pump-oxygenator components (McCaughan et al.), 210
Open heart operations, storage of blood for (Abbott et al.), 698
  surgery, use of hypothermia with cardiopulmonary bypass for (Su et al.), 1079
Outflow and inflow changes in ammonia concentrations of liver, muscle, and brain (Artz et al.), 22
Oxygen consumption, perfusion rate, and temperature, relationship of, to acidosis associated with cardiopulmonary circulatory bypass (Clowes et al.), 220
  tension, myocardial, and survival in acute hemorrhagic hypotension, l-norepinephrine in (Simeone et al.), 168

P

Pancreas, endocrine influences of, on gastric secretion; glucagon and alloxan in Heidenhain pouch secretion (Mayo and Enerson), 91
Pancreatic carcinoma, palliative biliary diversion for, duodenal obstruction appearing after (Pipes and Pareira), 636
  damage and serum desoxyribonuclease activity (Donahue et al.), 1070
Pancreatitis, relapsing, chronic, caudal pancreatojejunostomy in (Jordan and Howard), 303
Pancreatojejunostomy, caudal, in chronic relapsing pancreatitis (Jordan and Howard), 303
Paralysis, facial, anastomosis of branches of facial and spinal accessory nerves for (Caldwell), 978
Paraplegic patient, wound healing in (Localio et al.), 625
Parasitization of isolated small bowel loops in dogs (Miller et al.), 402
Parasympatholytic drugs, synthetic, certain, and belladonna alkaloids, antisecretory and vagolytic effects of (Trotti and Adriani), 515
Parotid tumors (Hutchinson and Kiriluk), 483
Pepsin and acid, comparative resistance of esophagus to (Adler et al.), 795
Peptic ulcer and benign pyloric stenosis, gastroenterostomy and gastrectomy for, gastric cancer after (Pack and Banner), 1024
  effect of cabbage factor on, of Mann-Williamson dogs (Baret et al.), 817
  perforated, management of (Berne and Mikkelson), 591

Perforated peptic ulcer, management of (Berne and Mikkelsen), 591
Perfusion rate, oxygen consumption, and temperature, relationship of, to acidosis associated with cardiopulmonary circulatory bypass (Clowes et al.), 220
transaortic coronary artery, needle to facilitate (Roe), 554
Peripheral blood, failure to prove identity of tumor cells in (Taylor and Vellios), 453
vascular response to arteriography, impedance plethysmography in evaluation of (Moore et al.), 345
Peritoneal fluid, toxicity of, resulting from strangulation obstruction, neomycin in (Barnett and Doyle), 442
Philosophy, surgical (Morton), 927
Phlebography, popliteal, in varicose vein problem (DeWeese), 390
Physical and biologic factors in impedance plethysmography (Powers et al.), 53
Plasma volume determination, methodologic and actual error of (Senn and Karlson), 1095
Plastic arterial grafts (B. rev.), 784
dressings versus fabric dressings (Hagerty and Jeffords), 556
surgical mask, comparative studies with (Kiser and Hitchcock), 936
Plethysmography, impedance, in evaluation of peripheral vascular response to arteriography (Moore et al.), 345
physical and biologic factors in (Powers et al.), 53
Plexiglas window for observation of intraperitoneal adhesions (Jackson), 507
Popliteal artery, distal, surgical exposure of (McCaughan), 536
phlebography in varicose vein problem (DeWeese), 390
Portograms, Urokon, in dogs (Pate), 570
Presidential address of Society of University Surgeons (Moore), 1
Pressure, blood, and venous return, arterenol in, during extracorporeal circulation (Herron et al.), 398
studies, reflux, on ileocecal valve of dogs and humans (Rendleman et al.), 640
Prostheses, Teflon-nylon, and aortic homografts in rabbit, effect of hypercholesterolemia on (Rustad et al.), 726
Prosthesis, arterial, nylon, new type of (Catchpole and Curran), 994
Pseudomembranous enterocolitis, fecal enema as adjunct to treatment of (Eiseman et al.), 854
Pulmonary hypertension, experimental production of (Barnes et al.), 361
stenosis with cyanosis following failure of systemic-pulmonary anastomoses, second shunting operations for (Haller), 919
in dogs, production and release of (Albert et al.), 904
Pulmonary—Cont'd
venous connection, anomalous, total (Longmire et al.), 572
Pump, occlusive, totally, use of, as a flowmeter with observations on hemolysis caused by occlusive and nonocclusive pumps and other pump-oxygenator components (McCaughan et al.), 210
-oxygenator system, survival of excised dog kidney perfused in; circulatory changes in hypothermic preparation (Couch et al.), 666
-oxygenators, experimental employment of, observed central nervous system responses during (Owens et al.), 240
Pyloric antrum, relative extent of distal gastrectomy necessary to insure complete extirpation of (Edit.), 775
stenosis, benign, and peptic ulcer, gastroenterostomy and gastrectomy for, gastric cancer after (Pack and Banner), 1024
Pyloroplasty, new technique of (Moschel et al.), 813
Pyridoxine deficiency in skin homograft survival (Fisher et al.), 149

R

Rayon dressings, fine mesh, comparison with perforated Mylar dressings (Hagerty and Jeffords), 556
Reconstruction, simultaneous, of breasts, mastectomies with (de Cholnoky), 689
Reconstructions, Billroth I and Billroth II (Herrington), 1040
Rectum and colon, multiple carcinomas of (McGregor and Bacon), 828
Reflux, gastroesophageal, and esophagitis, valve mechanism to prevent (Adler et al.), 63
pressure studies on ileocecal valve of dogs and humans (Rendleman et al.), 640
Regeneration, liver, in rat, possible humoral factors in (Smythe and Moore), 561
Regurgitation, mitral, direct vision correction of (Kay et al.), 325
Renal hypothermia, regional (Stueber et al.), 77
Resection, gastric, with end-to-end cholecystoduodenostomy in duodenal ulcer with obstruction to common bile duct (Hallenbeck), 850
of soft parts for sarcoma (Bowden and Booher), 963
Retrocostoxiphoid area, diaphragmatic deficiency in (Craighead and Strug), 1062
Retrosternal esophageal replacement employing jejunum or ileum (Jezioro and Kus), 275
Revascularization, myocardial, physiologic and anatomic determinants of coronary blood flow and their relationship to (Sabiston and Blalock), 406

Review of Society of University Surgeons meeting (Richards), 263
Riddle of stuttering, the (B. rev.), 433
Rudolph Matas history of medicine in Louisiana, the (B. rev.), 1118
Rupture of diaphragm, paradoxical motion of abdominal wall in (Lui et al.), 295

S

Sarcoma, resection of soft parts for (Bowden and Booher), 963
Sciatic nerve tension, flip sign in (Michele), 940
Secretion, gastric, and digestion, depression of, by gastric hypothermia in massive hematemesis (Wangensteen et al.), 265
endocrine influences of pancreas on; glucagon and alloxan in Heidenhain pouch secretion (Mayo and Enerson), 91
Section of sphincter of Oddi, risk of (Frieden and Shulman), 860
SGOT patterns following intracardiac surgery (Snyder et al.), 1083
Shunting operations, second, for pulmonary stenosis with cyanosis following failure of original systemic-pulmonary anastomoses (Haller), 919
Sigmoid diverticulitis, acute small bowel obstruction with, and its management (Bodon and Lapuz), 631
Skin grafts, transplantation of, from animals treated with 20-methylcholanthrene, induced lymphosarcoma from (Hardin et al.), 176
homograft survival, pyridoxine deficiency in (Fisher et al.), 149
Society of University Surgeons issue, 1-264
meeting, review of (Richards), 263
Soframycin, intestinal bactericide, preliminary studies on (Connell and Rousselot), 447
Sphincter, esophagogastric, substitution of, jejunal interposition operation for (Merendino and Thomas), 1112
of Oddi, risk of section of (Frieden and Shulman), 860
Spinal accessory and facial nerves, anastomosis of branches of, for facial paralysis (Caldwell), 978
Stenosis, aortic, congenital, treatment of, with valvotomy during cardiopulmonary bypass (Spencer et al.), 109
mitral, digital and instrumental commissurotomy in (Dogliotti et al.), 706
direct vision correction of (Kay et al.), 325
pulmonary, with cyanosis following failure of systemic-pulmonary anastomoses, second shunting operations for (Haller), 919
in dogs, production and release of (Albert et al.), 904
Stenosis—Cont'd
pyloric, benign, and peptic ulcer, gastroenterostomy and gastrectomy for, gastric cancer after (Pack and Banner), 1024
Stomach, complete exclusion of, in fat and nitrogen absorption (Plzak et al.), 299
duplication of (Thorbjarnarson and Haynes), 585
Storage of blood for open heart operations (Abbott et al.), 698
Stored cutaneous autografts in wound treatment (Feller and DeWeese), 540
Strangulation obstruction, neomycin in toxicity of peritoneal fluid resulting from (Barnett and Doyle), 442
Stress, various forms of, mast cell activity under (Villavicencio and de Takats), 312
Subphrenic abscess (Strode), 1054
Surgery, American, role of university in (Moore), 1
of the chest (B. rev.), 1118
Surgical infections, control of, at Minneapolis General Hospital (Hitchcock et al.), 492
mask, plastic, comparative studies with (Kiser and Hitchcock), 936
meetings, calendar of, 264, 434, 612, 765, 962
philosophy (Morton), 927
Sweat gland origin, carcinoma of (Moran and Horn), 683
Synthesis of urea and metabolic reactions of transaminase in ammonia intoxication (Najarian et al.), 11
Synthetic parasympatholytic drugs, certain, and belladonna alkaloids, antisecretory and vagolytic effects of (Trotti and Adriani), 515
Systemic-pulmonary anastomoses, failure of, second shunting operations for pulmonary stenosis with cyanosis following (Haller), 919

T

Teflon-nylon prostheses and aortic homografts in rabbit, effect of hypercholesterolemia on (Rustad et al.), 726
Temperature, oxygen consumption, and perfusion rate, relationship of, to acidosis associated with cardiopulmonary circulatory bypass (Clowes et al.), 220
Tensile strength of wounds in various nutritional deficiency states (Sisson et al.), 613
Tension, effect of, on healing of aponeurotic wounds (Thorngate and Ferguson), 619
myocardial oxygen, and survival in acute hemorrhagic hypotension, l-norepinephrine in (Simeone et al.), 168
Textbook of gynecology (B. rev.), 1119
Thoracic aorta grafts, atherosclerotic changes in (Flom et al.), 356

Tissue, soft, resection of, for sarcoma (Bowden and Booher), 963
Toxicity of peritoneal fluid resulting from strangulation obstruction, neomycin in (Barnett and Doyle), 442
Transaminase, metabolic reactions of, and synthesis of urea in ammonia intoxication (Najarian et al.), 11
serum, patterns after intracardiac surgery (Snyder et al.), 1083
Transplantation, heterologous, of human cancer in untreated Swiss-Webster mice (Richards and Klausner), 181
of skin grafts from animals treated with 20-methylcholanthrene, induced lymphosarcoma from (Hardin et al.), 176
Tumor cells in peripheral blood, failure to prove identity of (Taylor and Vellios), 453
Tumors, granulomatous, and neoplasms of colon and anorectal zone in Venezuela (de Bellard and Carreño), 627
parotid (Hutchinson and Kiriluk), 483

U

Ulcer, duodenal, with obstruction to common bile duct, gastric resection with end-to-end cholecystoduodenostomy in (Hallenbeck), 850
gastric (Bernardo et al.), 804
appraisal of treatment of (Welch and Burke), 943
gastrojejunal, presenting as mass in abdominal wall (Foster and Carlson), 1034
peptic, and benign pyloric stenosis, gastroenterostomy and gastrectomy for, gastric cancer after (Pack and Banner), 1024
effect of cabbage factor on, of Mann-Williamson dogs (Baret et al.), 817
perforated, management of (Berne and Mikkelsen), 591
Umbilical tape band, production of pulmonary stenosis by use of (Albert et al.), 904
University in American surgery (Moore), 1
Surgeons, Society of, issue, 1-264
meeting, review of (Richards), 263
Urea, synthesis of, and metabolic reactions of transaminase in ammonia intoxication (Najarian et al.), 11
Urinary diversion; metabolic alterations associated with use of isolated ileal segments (Staley and Scanlon), 646
tract metastases by cancers of large bowel (Majnarich and Malament), 520
Urokon portograms in dogs (Pate), 570

V

Vagolytic and antisecretory effects of belladonna alkaloids and certain synthetic parasympatholytic drugs (Trotti and Adriani), 515
Valve, ileocecal, of dogs and humans, reflux pressure studies on (Rendleman et al.), 640
mechanism to prevent gastroesophageal reflux and esophagitis (Adler et al.), 63
Valvotomy, treatment of congenital aortic stenosis with, during cardiopulmonary bypass (Spencer et al.), 109
Varices, carcinoma, and caustic atresia of esophagus, construction of new esophagus by means of transverse colon and its application for (Montenegro and Cutait), 785
Varicose vein problem, popliteal phlebography in (DeWeese), 390
Vascular response, peripheral, to arteriography, impedance plethysmography in evaluation of (Moore et al.), 345
Vein, varicose, problem, popliteal phlebography in (DeWeese), 390
Vena caval replacement, superior; successful use of fresh autogenous aorta (Moore and Riberi), 898
Venography, jugular, venous patterns following occlusion of jugular system demonstrated by (Cook et al.), 338
Venous-to-arterial bypass, femoral, as support of circulation in acute heart failure (Connolly et al.), 255
Venous connection, pulmonary, total anomalous (Longmire et al.), 572
patterns following occlusion of jugular system demonstrated by jugular venography (Cook et al.), 338
return and blood pressure, arterenol in, during extracorporeal circulation (Herron et al.), 398
Ventricular stimulation, monopolar, for control of acute surgically produced heart block (Brockman et al.), 910
Vitamin B_6 deficiency in skin homograft survival (Fisher et al.), 149
Volume, blood, constant, hemodynamic mechanisms which maintain, during cardiopulmonary bypass (Gianelli et al.), 378
plasma, determination, methodologic and actual error of (Senn and Karlson), 1095

W

Wound healing in paraplegic patient (Localio et al.), 625
response of injured tissues to coenzyme adenosine 5-monophosphate (Reynolds et al.), 33
in various nutritional deficiency states, comparison of (Sisson et al.), 613
treatment, stored cutaneous autografts in (Feller and DeWeese), 540
Wounds, aponeurotic, effect of tension on healing of (Thorngate and Ferguson), 619

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The Principles and Technique of Resection of Soft Parts for Sarcoma. Lemuel Bowden, M.D., and Robert J. Booher, M.D., New York, N. Y. ---- 963

Anastomosis of the Branches of the Facial and Spinal Accessory Nerves for Facial Paralysis. Elbert H. Caldwell, M.D., Tyler, Texas ---- 978

A Simple Technique for Endarterectomy. Harvey R. Butcher, Jr., M.D., St. Louis, Mo. ---- 984

A New Method of Artery Graft Anastomosis. John T. Phelan, M.D., Madison, Wis. 990

A New Type of Arterial Prosthesis. B. N. Catchpole, F.R.C.S., and R. C. Curran, M.D., Sheffield, England ---- 994

Pathologic and Radiographic Studies of Amputated Extremities. Falls B. Hershey, M.D., William O. Aikman, M.D., Lauren V. Ackerman, M.D., and Warren G. Stamp, M.D., St. Louis, Mo. ---- 1008

The Late Development of Gastric Cancer After Gastroenterostomy and Gastrectomy for Peptic Ulcer and Benign Pyloric Stenosis. George T. Pack, M.D., and Robert L. Banner, M.D., New York, N. Y. ---- 1024

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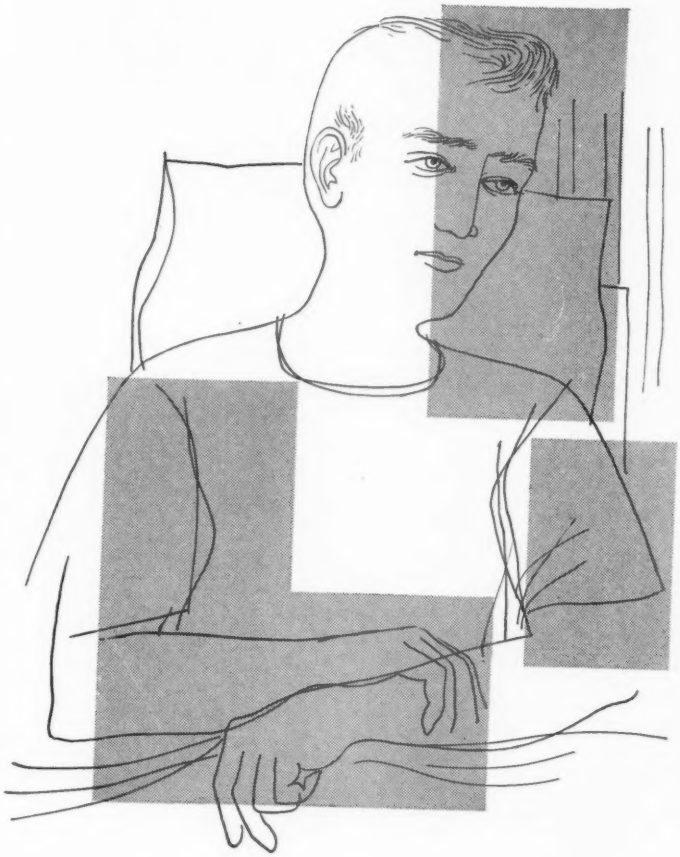

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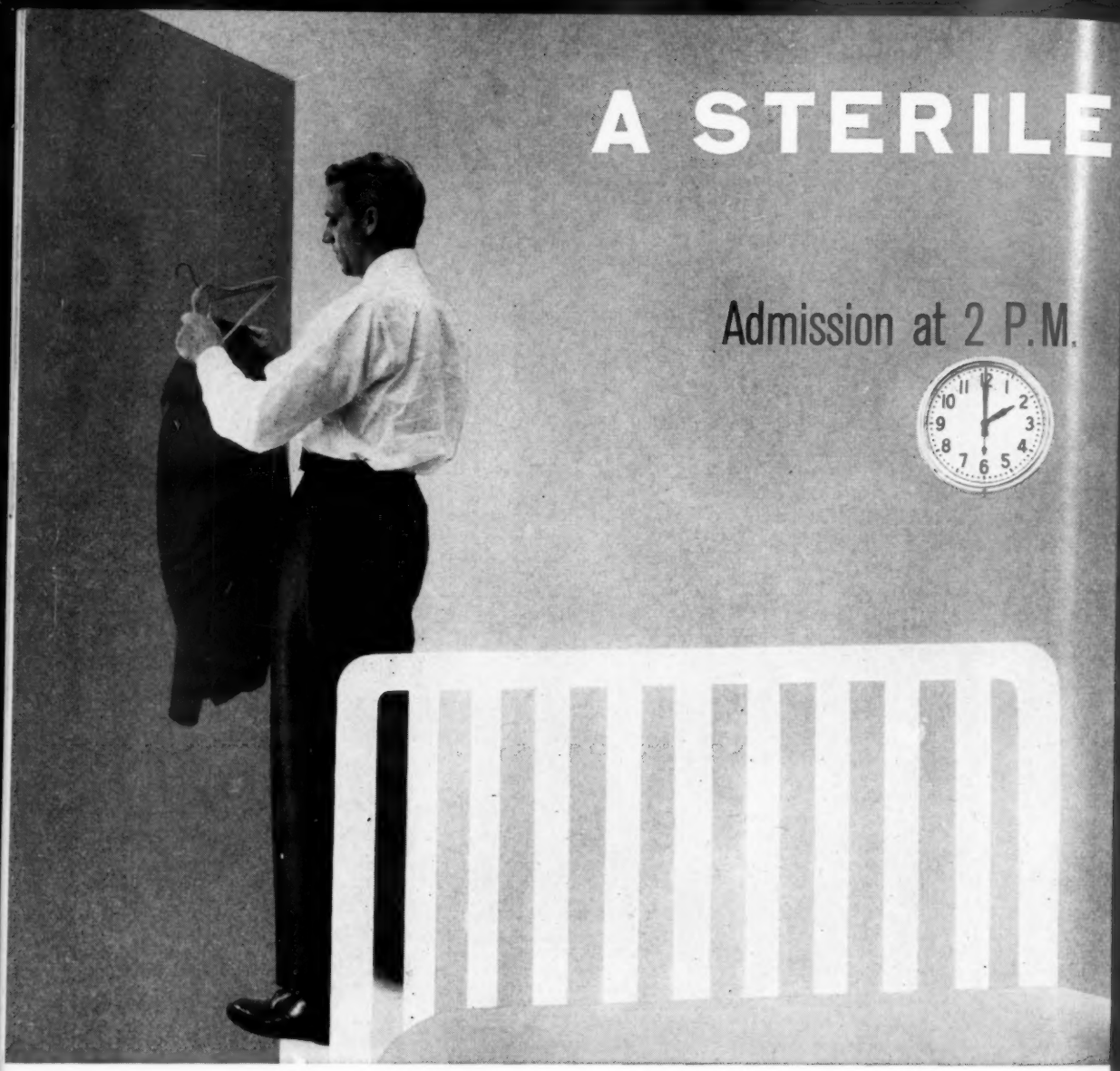

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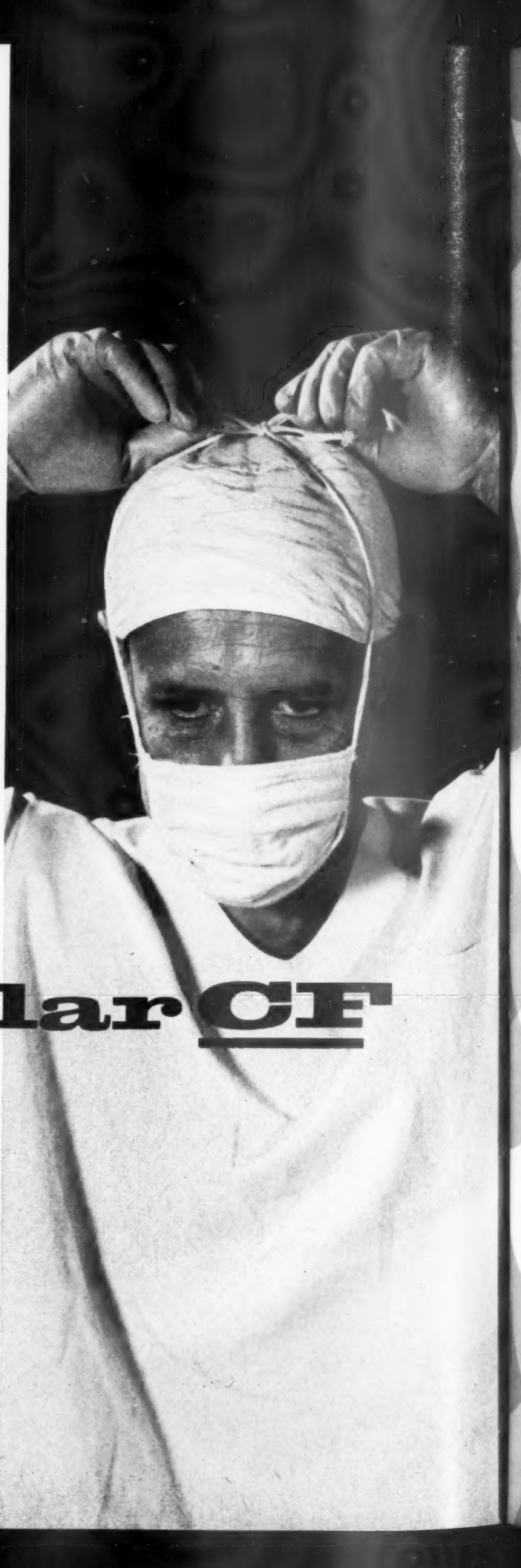

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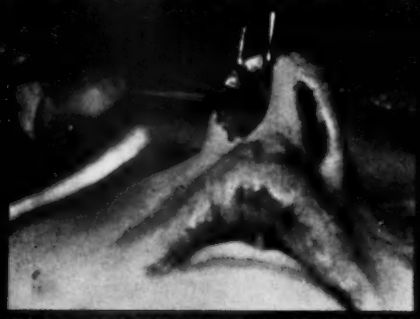

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1. Orzac, E.: Medical Care of the Child Patient Before and After Adenoidectomy and Tonsillectomy, N.Y. State J. Med. 56:886 (Mar., 1956).
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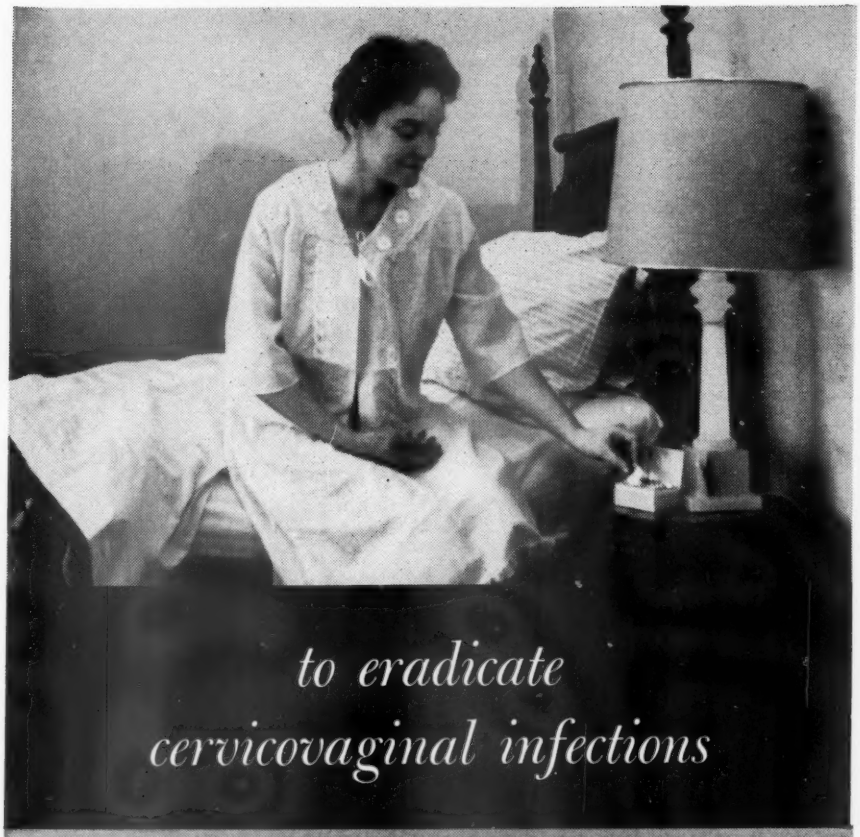

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1. Helms, W. C.: J. M. A. Georgia 42:376, 1953. 2. Rogers, S. F., and Moore, J.: Texas J. M. 53:338, 1957. 3. Schwartz, J.: Am. J. Obst. 63:579, 1952.

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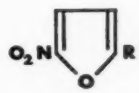

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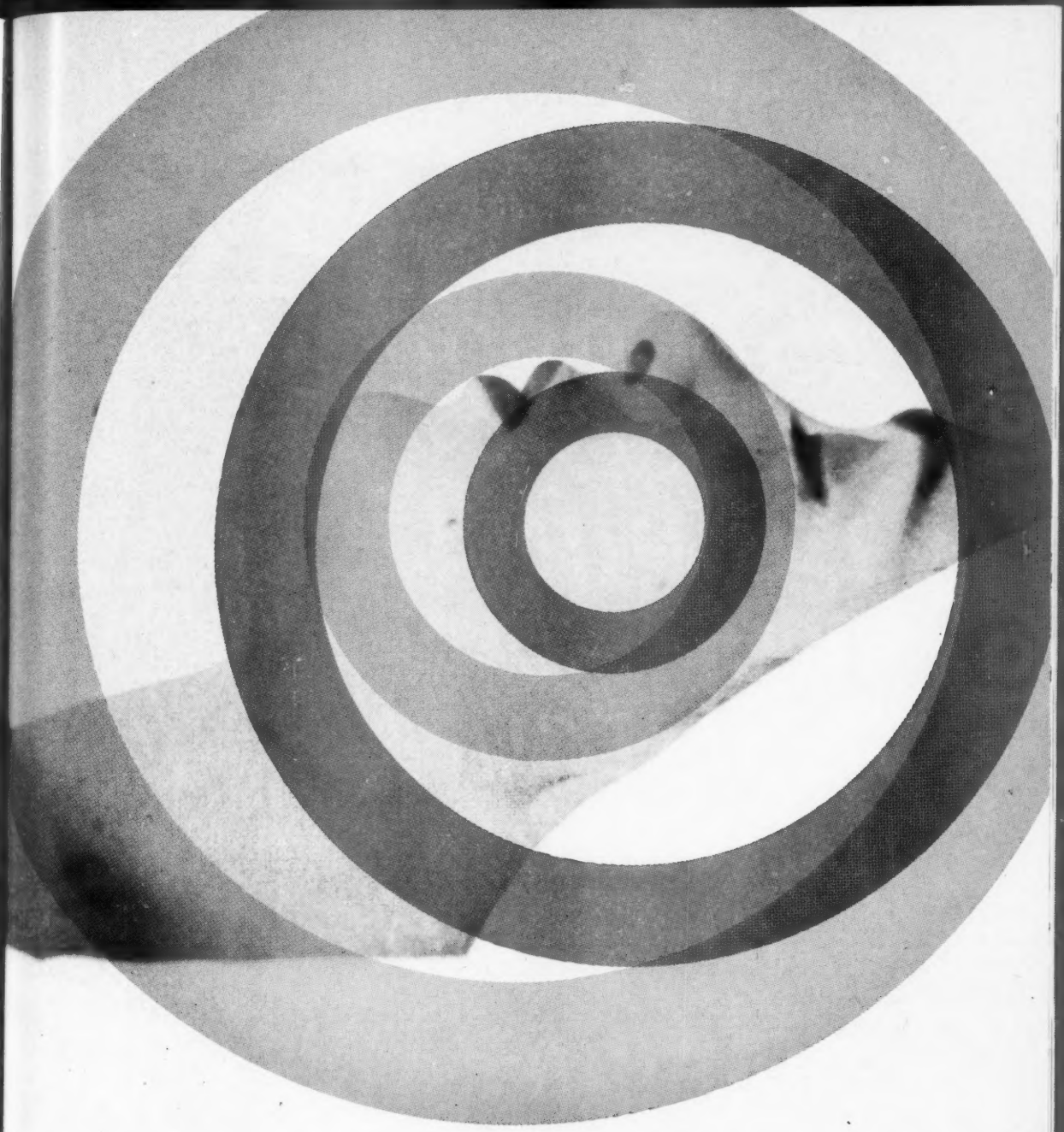

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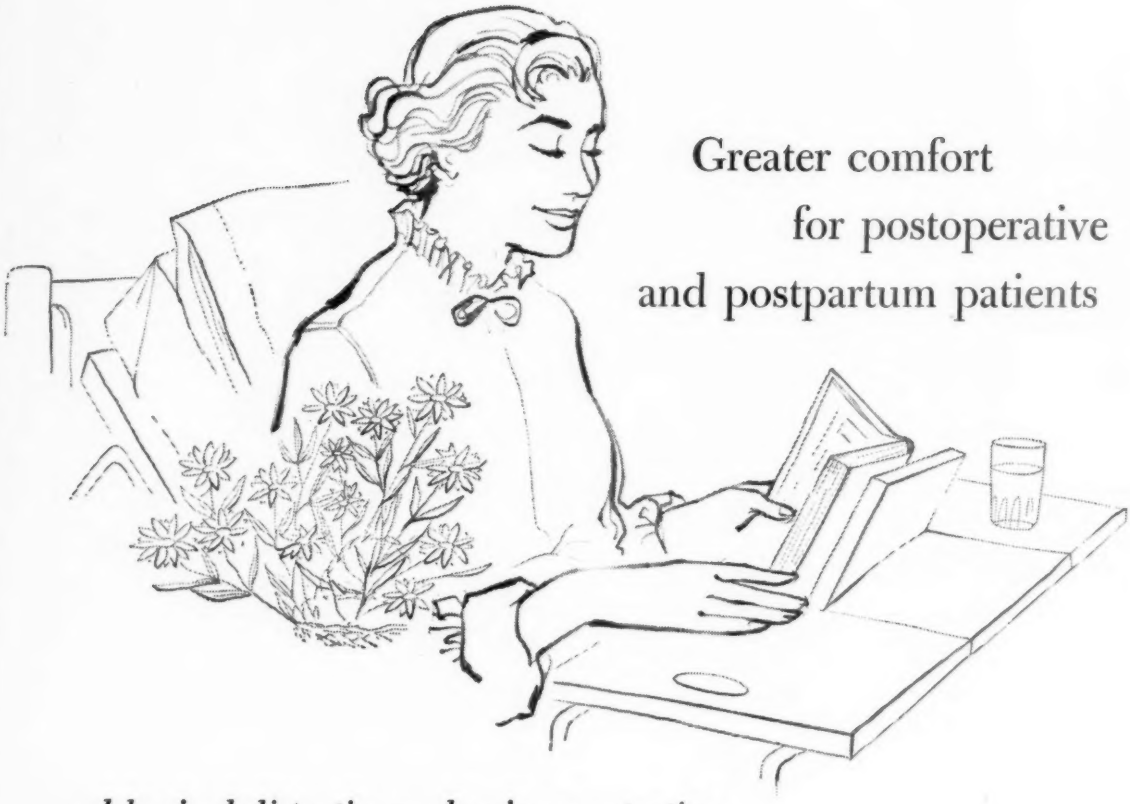

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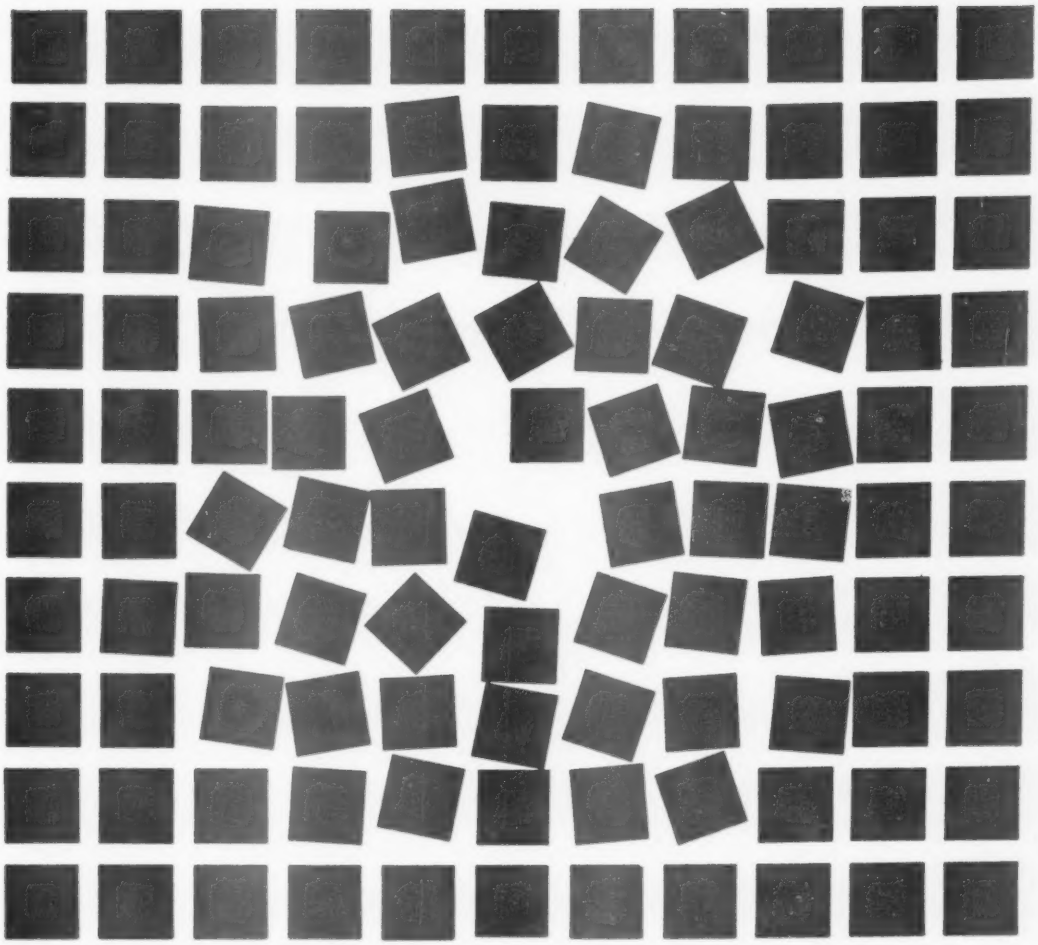

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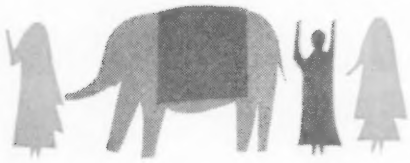

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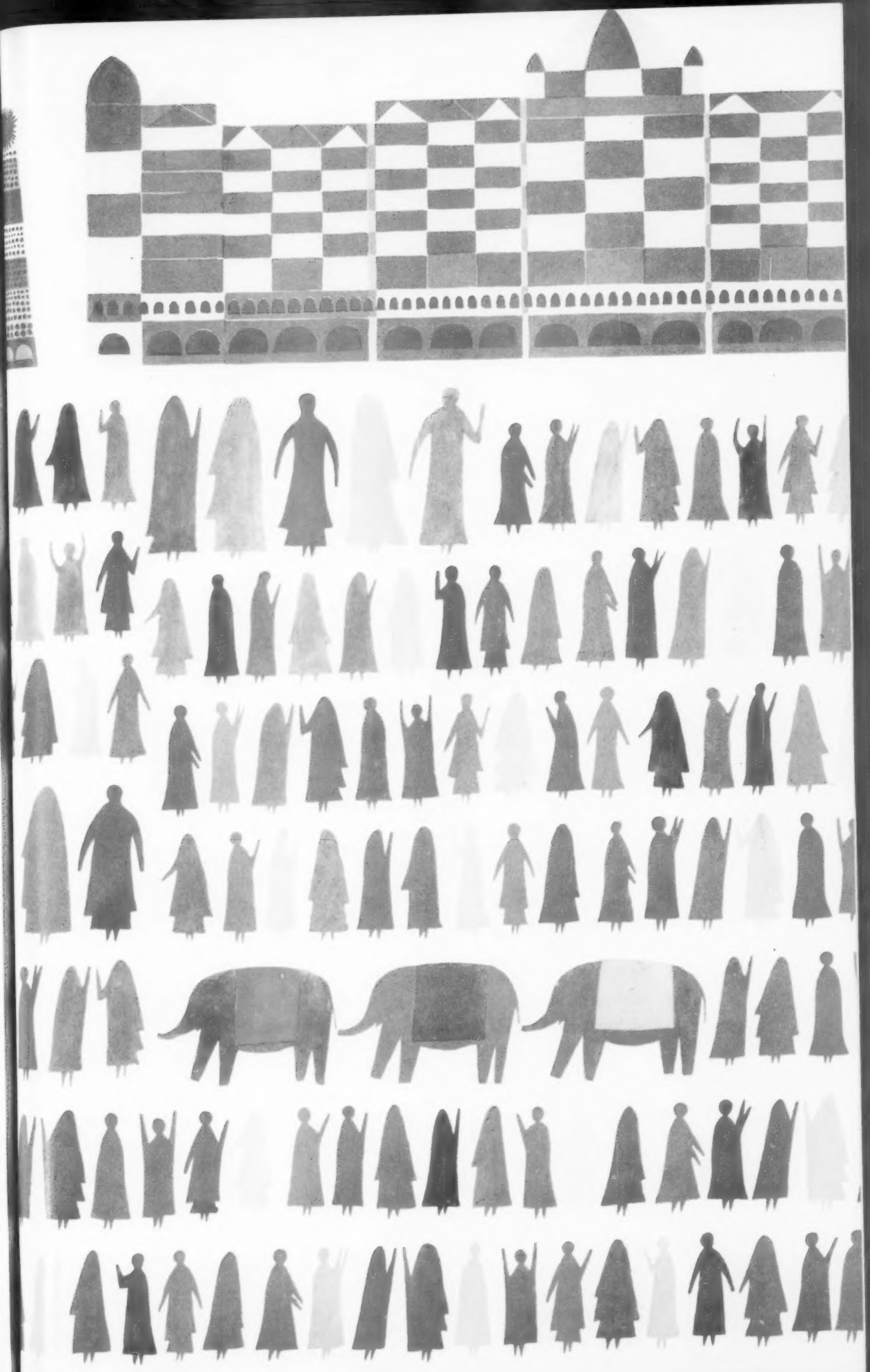

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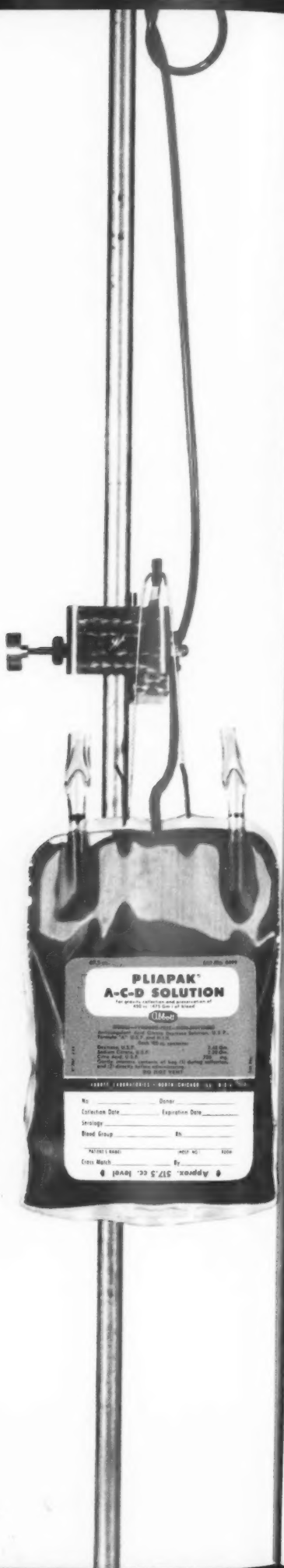

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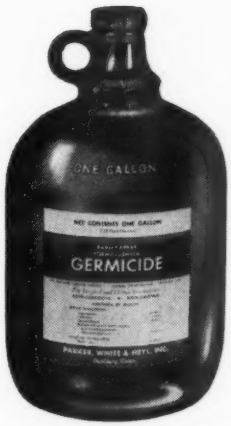

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Urological Surgery

by

AUSTIN INGRAM DODSON, M.D., F.A.C.S., Professor of Urology, Medical College of Virginia; Urologist to the Hospital Division, Medical College of Virginia; Urologist to Crippled Children's Hospital; Urologist to St. Luke's Hospital and McGuire Clinic, Richmond, Va. 3rd Ed. 868 pages. 664 illustrations. Price $20.00.

This book presents and discusses those surgical problems arising in everyday urological practice. The subject matter is arranged on an anatomical basis in the belief that an individual problem can be referred to more easily. Because in many communities urological surgery must be done by surgeons lacking a basic training in urology this book contains some discussion of diagnosis and pathology where such discussion will clarify the subject.

Three chapters occurring in the first and second editions have been eliminated so that additional surgical procedures and illustrations could be added. The problem of Acid-Base Balance and Fluid Administration has become too broad a subject to be treated adequately in a single chapter; furthermore, excellent monographs on the subject are now available. A brief discussion of this subject as well as Blood Transfusions and the Treatment of Shock is included in the chapter on Preoperative and Postoperative Care. Radiation Therapy, with the addition of new radioactive substances, has become too broad a subject to be adequately discussed in the space available.

The chapter on the Adrenal Glands and the Section on Ureterosigmoidostomy have been rewritten. The chapter on Neurogenic Diseases of the Bladder has been replaced by a chapter on Surgical Treatment of Urinary Tract Dysfunction Due to Disease or Injury of the Nervous System. This chapter deals chiefly with the urological rehabilitation of the paraplegic patient.

The section on Perineal Prostatectomy has been rewritten. In the chapter on Surgical Conditions of the Female Urethra and Their Treatment more attention is given the problem of Stress Incontinence, and operations found beneficial in the author's experience have been added.

Some changes have been made in many of the remaining chapters, consisting chiefly in the addition of surgical procedures or illustrations. A separate chapter has been added dealing with Postoperative Urinary Incontinence.

CHAPTER HEADINGS

Anatomy of the Urogenital Tract
Diagnosis
Preoperative and Postoperative Care of the Urological Patient (Charles M. Nelson)
Anesthesia in Urological Surgery (Williams E. Pemberton)
Surgical Approach to the Kidney. Incisions for Operations on the Kidney
Congenital Anomalies of the Kidney and Their Treatment
The Surgical Treatment of Renal Infections
Renal Tuberculosis and Its Treatment (T. Leon Howard)
Injuries of the Kidney and Their Treatment (George C. Prather)
Nephroptosis and Its Treatment
Renal Calculi and Their Treatment
Hydronephrosis: Surgical Treatment of Obstruction and the Ureteropelvic Juncture
Cysts of the Kidney and Their Treatment
Tumors of the Kidney and Their Treatment
Nephrectomy
Aneurysm of the Renal Artery
The Adrenal Glands (Austin I. Dodson, Jr.)
Surgical Approach to the Ureters, Incisions for Operations on Ureters
Congenital Anomalies of the Ureter and Their Treatment
Surgical Diseases of the Ureter and Their Treatment Ureteral Calculi and Their Treatment
Injuries of the Ureter and Their Treatment (George C. Prather)
Ureteral Anastomoses and Implantations
Tumors of the Ureter and Their Treatment. Ureterectomy
Surgical Approach to the Bladder, Incisions for Operations on the Bladder
Injuries of the Bladder and Their Treatment (George C. Prather)
Vesical Fistulas
Surgical Treatment of Urinary Tract Dysfunction Due to Disease or Injury of the Nervous System (R. Carl Bunts)
The Surgical Treatment of Patient Urachus, Cysts of Urachus, Exstrophy of Bladder and Diverticula of the Bladder
Tumors of the Bladder, General Considerations
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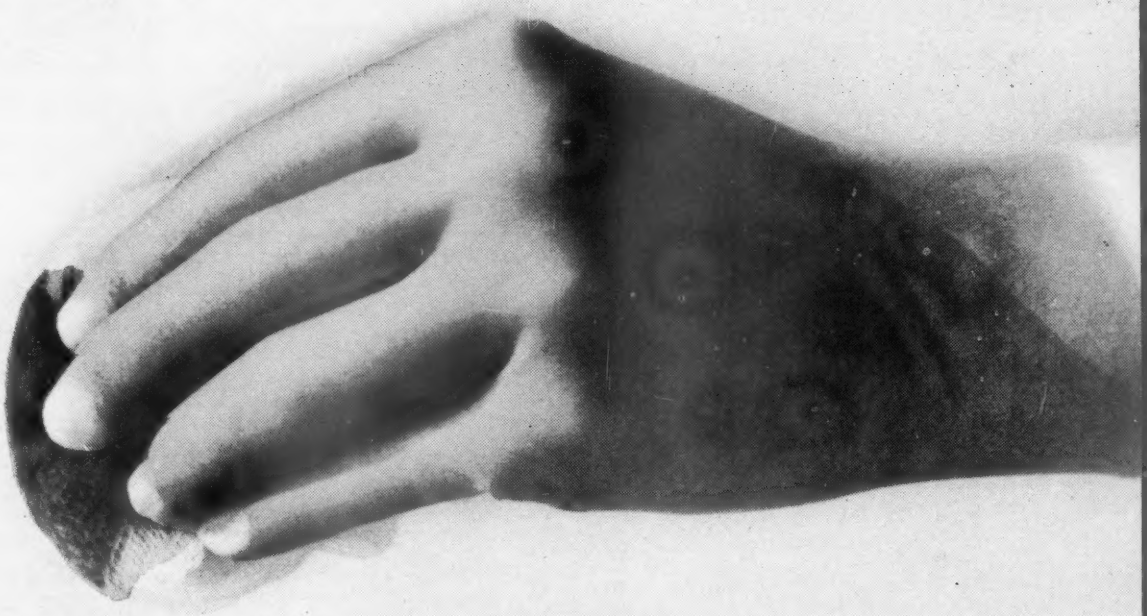

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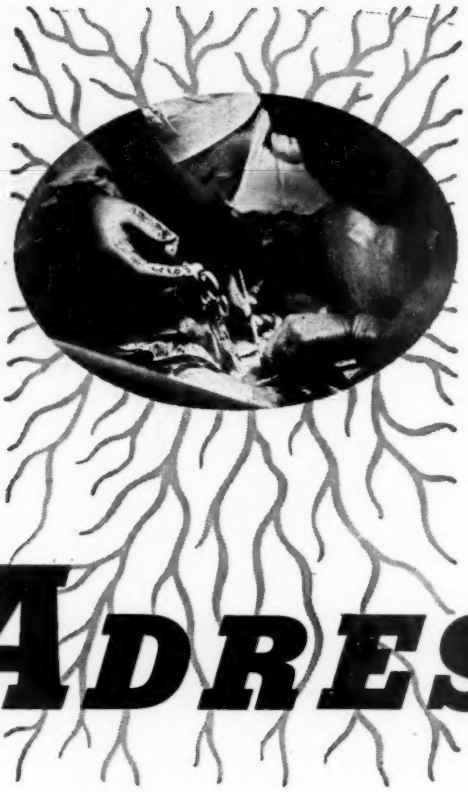

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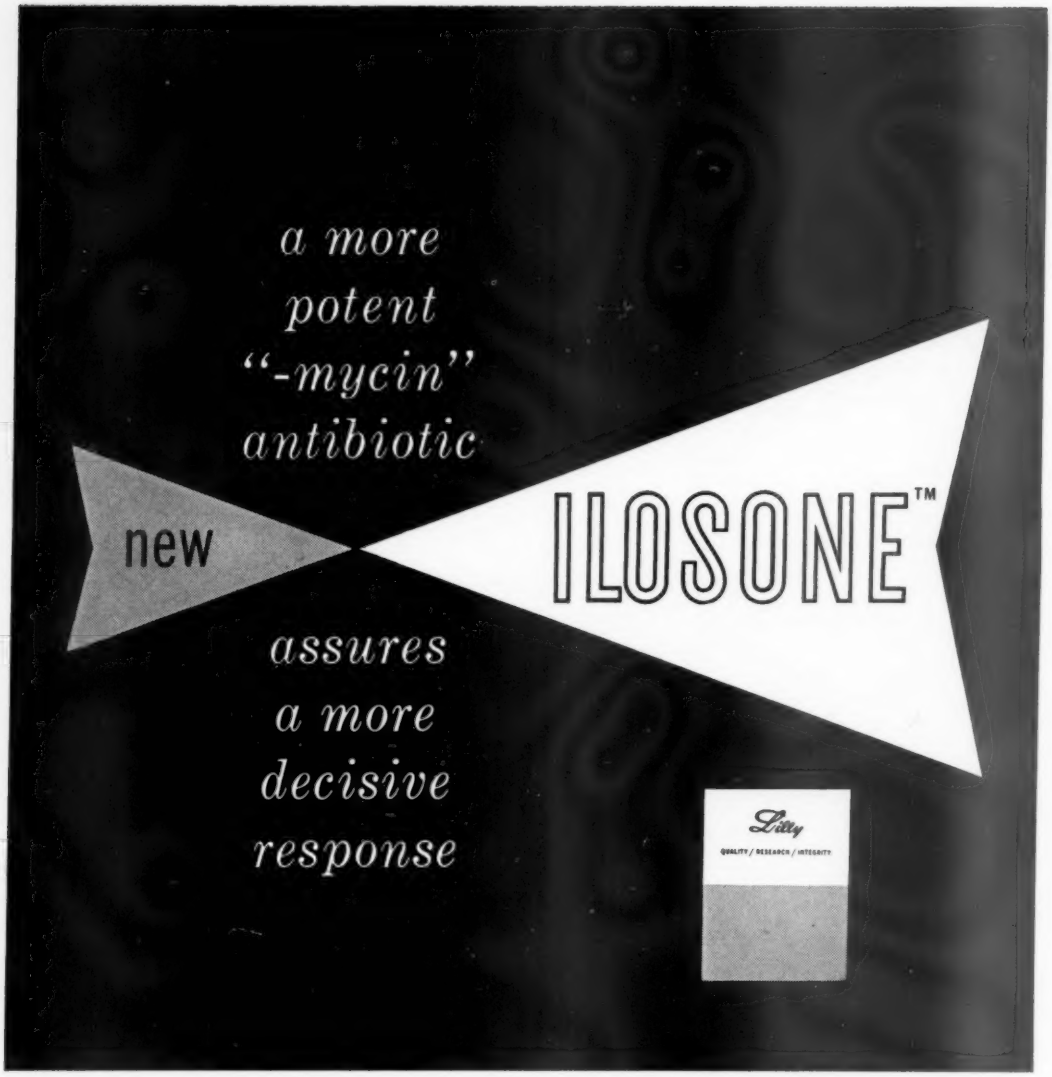

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ATLAS of GENERAL SURGERY

by

JOSEPH R. WILDER, M.D., Assistant Professor of Surgery, The New York Medical College, Flower and Fifth Avenue Hospitals, Assistant Attending, Metropolitan Hospital and The Bird S Coler Hospital, New York City; Formerly, Chief of the Surgical Services, The United States Air Force Hospital, Wright-Patterson Air Force Base, Dayton, Ohio.

1955, 222 pages, 10½" x 13½", 101 plates (700 step-by-step illustrations). **Price, $13.50**

From the Foreword

by FRANK GLENN, M.D.
Cornell University, Medical School

Craftsmanship is an integral part of successful surgery. Osler emphasized more than half a century ago that to study medicine without books was to sail an uncharted sea and that to study medicine with books but without patients was not to go to sea at all. Each surgeon must have one or more charted courses applicable to the objectives that he is approaching. It is not essential that his course follow that of another, so long as his "port" is reached with safety and maximum accomplishment of his patient.

The surgeon who knows well his course and can alter it skillfully and at will to meet the conditions encountered is the true master of his endeavor. AS CHARTS ARE TO THE NAVIGATOR SO ARE BOOKS AND DIAGRAMS TO THE SURGEON. For he who would know the art and craftsmanship of surgery, Dr. Wilder has provided on the following pages a series of line sketches portraying a simplified and direct approach for a wide range of surgical procedures. To this extent they represent an increasing trend in modern-day surgery to devote meticulous detail to the important and to avoid the superfluous.

This Atlas has been written with the objective of emphasizing selected techniques as performed within the confines of the operating room. Efforts have been directed toward explaining the techniques, difficulties, and possible complications one encounters in general surgery operations.

It covers all of the accepted general surgery procedures ranging from a minor operation to formidable major procedures such as: Cardiac Arrest, Radical Neck, Pancreatectomy, Removal of the Adrenal Glands, Pull Through Procedure, etc.

A multitude of methods are available for performing any operation. The techniques described in this book are those found most satisfactory by the author. Credit is not claimed for originating any of the techniques herein depicted. They represent accumulated knowledge from many sources, in large part from the teachers.

The illustrations resulted, with few exceptions, from the following approach: A rough draft of the anticipated operation was outlined prior to surgery. Using direct visualization in the operating room a second draft was prepared. This was carefully checked, teaching points emphasized, and the final drawings executed. In the more complicated procedures, numerous photographs were staged in the operating room, and postmortem dissections were performed to aid the artist in obtaining accuracy, perspective, and correct anatomical relationships. All efforts have been made to emphasize the exposures and anatomy as one actually encounters them in the operating room.

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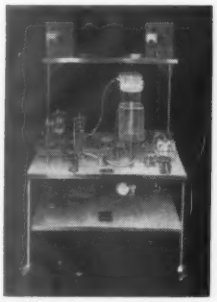

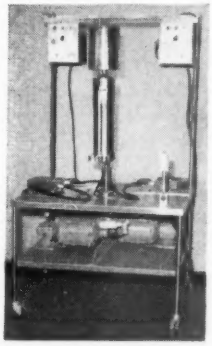

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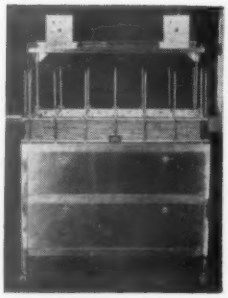

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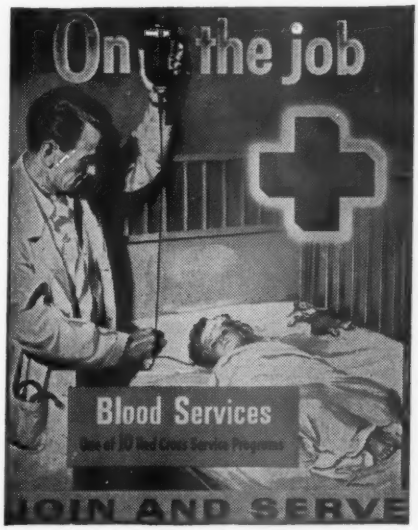

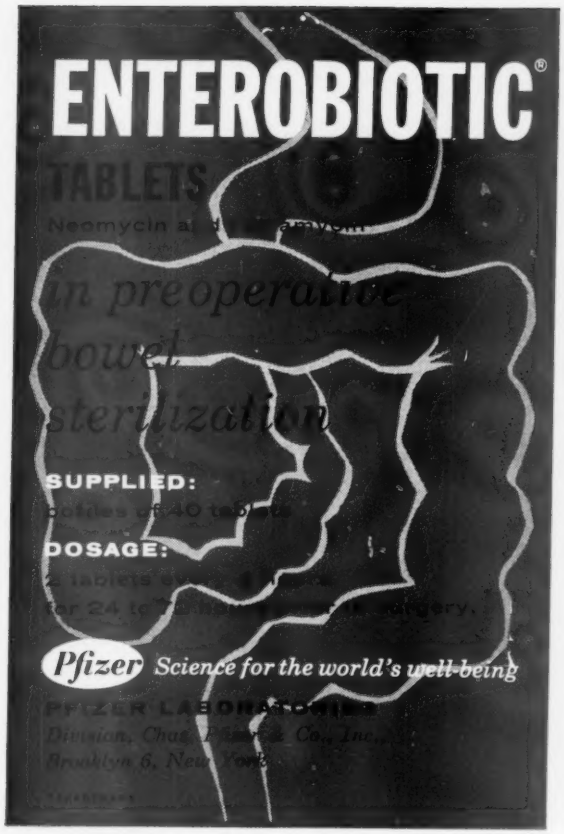

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W. A. D. ANDERSON, Professor of Pathology, University of Miami School of Medicine; Director of Pathology Laboratories, Jackson Memorial Hospital, Miami, Fla.

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Eaton Laboratories ---------- 9, 12

Ethicon, Inc. ---------- 10

Guardian Chemical Corporation ------ 21

Lederle Laboratories Division, American Cyanamid Company -------- 15, 25

Lilly and Company, Eli ---------- 24

March of Dimes, The ---------- 28

Mark Company, The ---------- 27

Massengill Company, The S. E. ------ ---------- Insert between pp. 8 and 9

Merck Sharp & Dohme ---- 6, 7, 14, 19, 34

Organon, Inc. ---------- 22

Parke, Davis & Company ---------- 11

Parker, White & Heyl, Inc. ---------- 17

Pfizer Laboratories, Div. Chas. Pfizer & Co., Inc. ---------- 27, 29

Roche Laboratories, Div. of Hoffmann-La Roche, Inc. ---------- 8

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The Billroth I and Billroth II Reconstructions. J. Lynwood Herrington, Jr., M.D., Nashville, Tenn. ---- 1040

Subphrenic Abscess. J. E. Strode, M.D., Honolulu, T. H. ---- 1054

Diaphragmatic Deficiency in the Retrocostoxiphoid Area. Claude C. Craighead, M.D., and Lawrence H. Strug, M.D., New Orleans, La. ---- 1062

Serum Desoxyribonuclease Activity and Pancreatic Damage. J. K. Donahue, M.D., J. C. Houck, Ph.D., and R. J. Coffey, M.D., Washington, D. C. ---- 1070

The Use of Hypothermia With Cardiopulmonary Bypass for Open Heart Surgery. Chien Sheng Su, M.D., Robert Hardin, M.D., and Harold King, M.D., Indianapolis, Ind. ---- 1079

Serum Transaminase Patterns Following Intracardiac Surgery. David D. Snyder, M.D., Christiaan N. Barnard, M.D., Richard L. Varco, M.D., Ph.D., and C. Walton Lillehei, M.D., Ph.D., Minneapolis, Minn. With the Technical Assistance of Miss Irene Bossenmaier ---- 1083

Prophylactic Treatment of the Murphy Sturm Rat Lymphosarcoma With Nitrogen Mustard. Kenneth Jackson, M.D., Elizabeth McGrew, M.D., and Warren H. Cole, M.D., Chicago, Ill. ---- 1092

Methodologic and Actual Error of Plasma Volume Determination. LaVonne Y. Senn, B.A., and Karl E. Karlson, M.D., Brooklyn, N. Y. ---- 1095

Pediatric Surgery

Intrauterine Intussusception as a Cause of Intestinal Atresia. K. V. Parkkulainen, M.D., Helsinki, Finland ---- 1106

Reappraisal

The Jejunal Interposition Operation for Substitution of the Esophagogastric Sphincter. K. Alvin Merendino, M.D., and George I. Thomas, M.D., Seattle, Wash. ---- 1112

In Memoriam

Arthur Wilburn Allen. Alton Ochsner ---- 1116

Book Reviews

Book Reviews ---- 1118

Index

Index ---- 1121

(Editorial and Business Communications on page 4)

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